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BILATERAL ENDOPHTHALMITIS COMPLICATING PNEUMOCOCCIC SEPTICEMIA

REPORT OF A CASE

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We are presenting this case of bilateral endophthalmitis because it is an instance of an ocular lesion occurring as the first manifestation of a generalized septicemia. It also affords a basis for discussion of metastatic ocular infections.

REPORT OF CASE

E. P., a 48 year old man, an upholsterer, had been in good health until Dec. 1, 1937, when he stepped on a tack while at work. This was followed by a local infection and lymphangitis of the left foot and lower part of the leg, for which he was treated by his family physician. A roentgenogram taken at the time showed no involvement of bone.

The patient appeared to be making a satisfactory recovery, all local signs and symptoms having disappeared, when, on December 15, he experienced severe frontal headache and became aware of a dimness of vision in each eye. The next day the periorbital tissues became swollen, and the patient experienced some pain in the eyes. At this time he had a slight chill and rise in temperature. He was seen in ophthalmologic consultation on December 17, when the eyes showed a typical picture of endophthalmitis, there being marked edema of the lids and chemosis of the bulbar conjunctiva. The corneas were hazy and the pupils small, irregular and fixed. Many posterior synechiae were present, and the iris structures were hemorrhagic. No view of the fundus was obtainable. Vision was reduced to perception of light.

The patient was immediately admitted to the University Hospital to the service of Dr. F. H. Adler. On his admission the temperature was 103 F. rectally. General physical examination, aside from examination of the eyes, showed the following positive findings: There were a few carious teeth. The heart was enlarged to the left. A systolic murmur and thrill were made out at the apex. The spleen was enlarged. There was slight tenderness over the medial aspect of the ball of the left foot but no inflammatory signs. The past medical history

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included typhoid fifteen years previously and pneumonia a number of years later. The family history was irrelevant.

It was felt that we were dealing with bilateral endophthalmitis of a metastatic nature, secondary to a septic focus, and the patient was studied from this point of view. The blood count showed 20,500 white cells, with 82 per cent polymorphonuclear cells. Urinalysis showed some albumin and occasional red blood cells. The Kolmer and Kahn reactions were negative. A roentgenogram of the chest showed no evidence of pulmonary consolidation. Roentgen studies of the sinuses showed bilateral clouding of the ethmoid sinuses. The consulting otolaryngologist did not consider the upper part of the respiratory tract to be a focus of infection. Examination of the spinal fluid was essentially negative. A blood culture taken on the patient's admission was reported to be positive for the type XVI pneumococcus, thus corroborating the initial impression of septicemia.

The patient failed progressively. The temperature assumed the appearance of a septic type, with the peaks gradually rising from 101 to 105 F. The inflammatory condition about the eyes subsided gradually, the chemosis disappeared, and the eyeballs began to undergo phthisic changes, vision being reduced to perception of light.

Treatment consisted first of the administration of sulfanilamide, the patient receiving a total of 390 grains (25.27 gm.) over a period of ten days. He was given daily transfusions of 200 cc. of citrated blood. Ethylhydrocupreine hydrochloride was also administered by mouth with the hope that it might have a specific effect on the pneumococcus.

Therapy was of no avail. The blood remained consistently positive for pneumococci, many colonies being isolated on each culture. A culture taken from the conjunctiva was negative. A culture from the nose grew Staphylococcus aureus. On Jan. 2, 1938, auricular fibrillation developed, and the patient died on January 7.

At autopsy the following significant changes were observed: multiple infarctions of the spleen and kidneys; patchy bronchopneumonia of the lungs; some soft vegetations on the mitral valve, representing a recent endocarditis, and phlebitis of the left femoral vein, probably secondary to the infection in the foot. Obviously this was the septic focus.

The left eye was removed, aspiration being done previously. The fluid obtained for culture was positive for the type XVI pneumococcus. The pathologic report on the globe follows: Grossly, the eye was rather small and distorted and was filled with a white exudate. Microscopic examination showed a purulent focus in the posterior part of the choroid; a purulent exudate with numerous macrophages had separated the retina, some of which was destroyed, and almost filled the vitreous; here the choroid was not purulent, and there were lymphocytes and plasma cells in its meshes, a septic choroiditis. Other changes observed were edema of the ciliary body; numerous leukocytes pouring from the ciliary epithelium; posterior synechia; a fibrous pupillary membrane; peripheral anterior synechia; optic neuritis, and septic thrombi in the arterioles of the retina. A diagnosis of metastatic purulent endophthalmitis was made.

COMMENT

Ocular infections of metastatic origin are, of course, not infrequent, and the case reported is unusual only from the standpoint of bilateral involvement and also because the ocular signs and symptoms constituted the first warning of the existence of the infection of the blood stream.

Metastatic panophthalmitis and endophthalmitis have been reported by various authors in the literature and ascribed to various foci.

Sherer [1] stated that systemic infections may cause any one of the following manifestations in the eye: (1) iridocyclitis, (2) metastatic ophthalmitis, (3) septic retinitis of Roth and (4) ring abscess of the cornea. He cited Groenouw, who collected 166 cases of metastatic lesions in the eye due to general sepsis. Of the cases of bilateral involvement in this series, 85 per cent were fatal. Bilateral involvement was present in 27 of Leber's series of 67 cases. Friedenwald and Rones [2] studied 32 cases of septicemia, routinely removing one eye at autopsy in each case. They found focal areas of choroiditis in 9 eyes in which no signs of ocular involvement had been noted during life. The offending organism in 1 case of endocarditis and septicemia was the type II pneumococcus.

Brazeau's [3] case was one of panophthalmitis secondary to an acute empyema of the gallbladder. Laval [4] described 2 cases of metastatic panophthalmitis resulting from carbuncles of the face, Staph. aureus being isolated. Hulka [5] described a case of pneumonia complicated by metastatic uveitis. In Levine's [6] case of metastatic ophthalmitis due to Bacillus coli the primary focus was a pyonephrosis.

Of all the cases cited, that reported by Conway [7] is the most analogous to ours. His patient was a coal miner who sustained a crushing injury to a finger. This led to the development of a general infection and bilateral endophthalmitis, followed by pneumonia and death. No blood culture was reported, but it would seem that the patient undoubtedly had a pneumococcic septicemia.

The physical factor for the production of the septic choroiditis or retinitis, as the case may be, is the lodging of circulating organisms in either a ciliary or a retinal artery. These infected emboli set up a localized purulent inflammation, which, if it involves the coats of the eyeball and the surrounding orbital tissues, often results in spontaneous rupture of the sclera.

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1. Sherer, J. W.: J. Missouri M. A. **24**:294 (July) 1927.

2. Friedenwald, J. S., and Rones, B.: Some Ocular Lesions in Septicemia, Arch. Ophth. **5**:175 (Feb.) 1931.

3. Brazeau, G. N.: Am. J. Ophth. **10**:685 (Sept.) 1927.

4. Laval, J.: Metastatic Panophthalmitis from Pyogenic Cutaneous Infections, Arch. Ophth. **18**:104 (July) 1937.

5. Hulka, J. H.: Metastatic Pneumococcic Uveoscleritis Following Pneumonia, Arch. Ophth. **17**:127 (Jan.) 1937.

6. Levine, J.: Metastatic Bacillus Coli Panophthalmitis from Calculus Pyonephrosis, Arch. Ophth. **3**:410 (April) 1930.

7. Conway, J. A.: Glasgow M. J. **118**:266 (Oct.) 1932.

Of the foregoing citations, only the most recent papers contained a report of bacteriologic studies. Lundsgaard [8] reviewed the role of the pneumococcus in connection with ophthalmic conditions. He stated that, generally speaking, a pneumococcic infection of the conjunctiva is acute and benign; of the lacrimal passages, chronic and fairly benign; of the cornea, acute and malignant. This review is largely concerned with corneal ulcer.

Newman [9] made a bacteriologic study in 100 cases of ocular disease. In his series there were 3 cases of panophthalmitis, the condition in 2 being due to the type III and type X pneumococcus and in 1 to Streptococcus viridans. Newman compiled a table showing the types of pneumococcus demonstrated in ocular disease by a large series of authors. He showed that only 25 per cent of the pneumococci occurring in ocular disease belong to types I, II and III and that 75 per cent are of type IV. As is known, type IV is divided into many subtypes, of which type XVI, the organism isolated in our case, is one. In all, there are 32 culturally distinct types of pneumococcus, for many of which therapeutic serum is available.

Unfortunately, no such serum was commercially obtainable for our patient. Since it is known that ethylhydrocupreine hydrochloride is lethal for the pneumococcus in vitro, this drug was utilized in our case. In the presence of the extensive infection of the blood stream, it was without effect.

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8. Lundsgaard, K. K.: Tr. Ophth. Soc. U. Kingdom **47**:294, 1927.

9. Newman, E. W.: Diplococcus Pneumoniae and Streptococcus Viridans in Ocular Diseases: Report of One Hundred Cases, Arch. Ophth. **19**:95 (Jan.) 1938.

THE RICKETTSIA QUESTION IN TRACHOMA

I. MICROSCOPIC OBSERVATIONS ON THE VIRUS

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Trachoma, a protean disease of the conjunctiva and cornea, has been known since the time of Hippocrates. Hirschberg [1] in 1904 stated that entire libraries have been written concerning the disease. Scientific experiments have been carried on for over a century, but trachoma still remains a dark chapter in ophthalmology.

Opinions as to the etiologic factors, the pathologic process and clinical picture of trachoma have been so contradictory that it is impossible to believe all that is written concerning the disease. Before the discovery of the inclusion bodies by Halberstädter and Prowazek [2] many micro-organisms found in the conjunctiva were suspected of being causative agents. With this momentous discovery, new impetus was gained and many publications appeared. In 1928 Noguchi [3] described a small rodshaped micro-organism which he named Bacterium granulosis; this organism caused a follicular conjunctivitis in monkeys which was thought to be trachoma; however, it did not cause trachoma in human subjects (Wilson;[4] Proctor, Finnoff and Thygeson;[5] Thygeson;[6] Nicolle and Lumbroso,[7] and others).

In 1930 Weiss reviewed the causation of trachoma and eliminated all previously described etiologic agents, including Bact. granulosis and the Halberstädter-Prowazek inclusion body.

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1. Hirschberg, J.: Klin. Jahrb. **13**:389, 1904.

2. Halberstädter, K., and von Prowazek, S.: Deutsche med. Wchnschr. **33**: 1285, 1907.

3. Noguchi, H.: J. Exper. Med. (supp. 2) **48**:1, 1928.

4. Wilson, R. P.: Brit. J. Ophth. **15**:433, 1931.

5. Proctor, F. I.; Finnoff, W. C., and Thygeson, P.: Am. J. Ophth. **15**:206, 1932.

6. Thygeson, P.: Role of Bacterium Granulosis in Trachoma, Arch. Ophth. **10**:1 (July) 1933.

7. Nicolle, E., and Lumbroso, V.: Arch. Inst. Pasteur de Tunis **20**:239, 1931

In 1935 Thygeson, Proctor and Richards [8] produced typical trachoma in a normal eye with material filtered through a graded collodion membrane with an average pore diameter of 0.6 micron. This result, associated with the facts that bacteria-free trachomatous material was capable of inducing infection in monkeys (Julianelle and Harrison [9]) and that bacteria plays a negative role in trachoma,[10] leads one to believe that trachoma is caused by a filtrable substance. Thygeson [11] in 1936 stated that "recent studies support the conclusion that trachoma is a virus disease" and that "evidence has been advanced which identifies the elementary body of Halberstädter and Prowazek with trachoma virus." The question of the elementary body being the trachoma virus has been the subject of a great many publications. Opinions have been divided, but at the present time it is believed that the elementary body represents the virus.

In 1933 Busacca [12] first described minute bodies in the cytoplasm of conjunctival cells from trachomatous material which he called rickettsias. Later, similar findings were reported by Cuénod and Nataf,[13] Foley and Parrot [14] and Poleff.[15] Thygeson [16] examined stained specimens of Cuénod and Nataf and both stained and unstained specimens of Busacca but was unable to demonstrate bodies that were similar to rickettsias. He concluded that the minute bodies observed were not the elementary bodies but cell granules and cytoplasmic débris. Grüter [17] considered the "rickettsias of trachoma" to be inflammatory proliferations and divisions of granules occurring normally in epithelial cells.

MATERIAL AND METHOD OF STUDY

A comparative study of smear preparations fixed in absolute methyl alcohol and stained by the method of Giemsa [18] was made of the epithelial cells from normal, nontrachomatous and trachomatous conjunctivas. Conjunctivas which did not give rise to any subjective or objective symptoms were considered normal. Conjunc-

8. Thygeson, P.; Proctor, F. I., and Richards, P.: Am. J. Ophth. **18**:811, 1935.

9. Julianelle, L. A., and Harrison, R. W.: Tr. Am. Acad. Ophth. **40**:221, 1935.

10. Stewart, F. H., in Eighth Annual Report of the Giza Memorial Ophthalmic Laboratory, Cairo, Schindler's Press, 1934, p. 142. Thygeson, P.: Arch. Inst. Pasteur de Tunis **22**:157, 1933.

11. Thygeson, P.: Am. J. Ophth. **19**:649, 1936.

12. Busacca, A.: Klin. Monatsbl. f. Augenh. **91**:277, 1933.

13. Cuénod, A.: Arch. d'opht. **52**:145, 1935. Cuénod, A., and Nataf, R.: ibid. **52**:573, 1935.

14. Foley, H., and Parrot, L.: Compt. rend. Soc. de biol. **124**:230, 1937.

15. Poleff, L.: Arch. d'opht. **53**:882, 1936.

16. Thygeson, P.: Problem of Rickettsias in Trachoma, Arch. Ophth. **20**:16 (July) 1938.

17. Grüter, W.: Rev. internat. du trachome **15**:9, 1938.

18. From 15 to 20 drops of Giemsa stain is added to 40 cc. of neutral distilled water, and the preparation is stained for one hour at 37 C.

tivas with acute or chronic bacterial conjunctivitis but showing no inclusion bodies were considered nontrachomatous. Conjunctivas with changes incident to exposure, e. g., ectropion, were also considered nontrachomatous. A diagnosis of trachoma was made when clinically the upper tarsus and retrotarsal fold showed follicles or papillary hypertrophy with an accompanying pannus of the cornea and when microscopic study of smears showed the Halberstädter-Prowazek inclusion bodies.

Normal conjunctival epithelium was removed, suspended in Tyrode's solution and studied immediately under bright and under dark field illumination. These cells were compared with epithelial cells obtained in a similar manner from trachomatous conjunctivas.[19]

RESULTS

Epithelium removed from normal conjunctivas and from conjunctivas with nontrachomatous inflammation when stained by Giemsa's method showed two types of granules in the cytoplasm.

The granules of one type (fig. 1 *A*) varied in size and shape and were irregularly scattered throughout the cytoplasm. In the deeper cells of the conjunctiva the granules were small and dustlike (fig. 1 *B*), while in the more superficial layers they tended to be larger and more discrete. The dustlike particles in the cytoplasm usually stained blue with the Giemsa method and in some instances gave to the cytoplasm a uniform pale blue appearance. When these granules were compared with those found under dark field illumination (fig. 1 *C*) they showed similar distribution and structure. The granules disappeared on the addition of dilute acetic acid and therefore undoubtedly were mitochondria.

The other type of granules, especially those seen in the superficial epithelial cells, were larger and did not disappear on the addition of dilute acetic acid (fig. 1 *D*). Such granules are undoubtedly closely allied to so-called keratin. With the Giemsa method these granules usually stained a pale pink (fig. 1 *E*) but were sometimes purple, the color depending on the hydrogen ion concentration of the staining solution. These larger granules of the conjunctival cells were more numerous in trachomatous material than in epithelium from the normal conjunctiva. If such granules are closely allied to keratin, they should be more numerous in the trachomatous than in the normal conjunctiva because in the former the epithelium becomes thickened and the surface cells may desquamate. These cells also showed a marked tendency to keratinize, while the normal conjunctival epithelium contained only small amounts of keratin. The tendency to extensive keratinization was also found in cases of long-standing chronic conjunctivitis and

19. The trachomatous material was obtained at Fort Apache, Ariz., on the Fort Apache Indian Reservation, through cooperation with the Health Division, Office of Indian Affairs, Department of the Interior, Washington, D. C.

especially in cases of ectropion. Dark field examination of the epithelial cells in the latter cases showed large amounts of coarse mitochondria in the cytoplasm. These granules were similar to the bodies described as rickettsias by Busacca,[12] Cuénod and Nataf [13] and others.

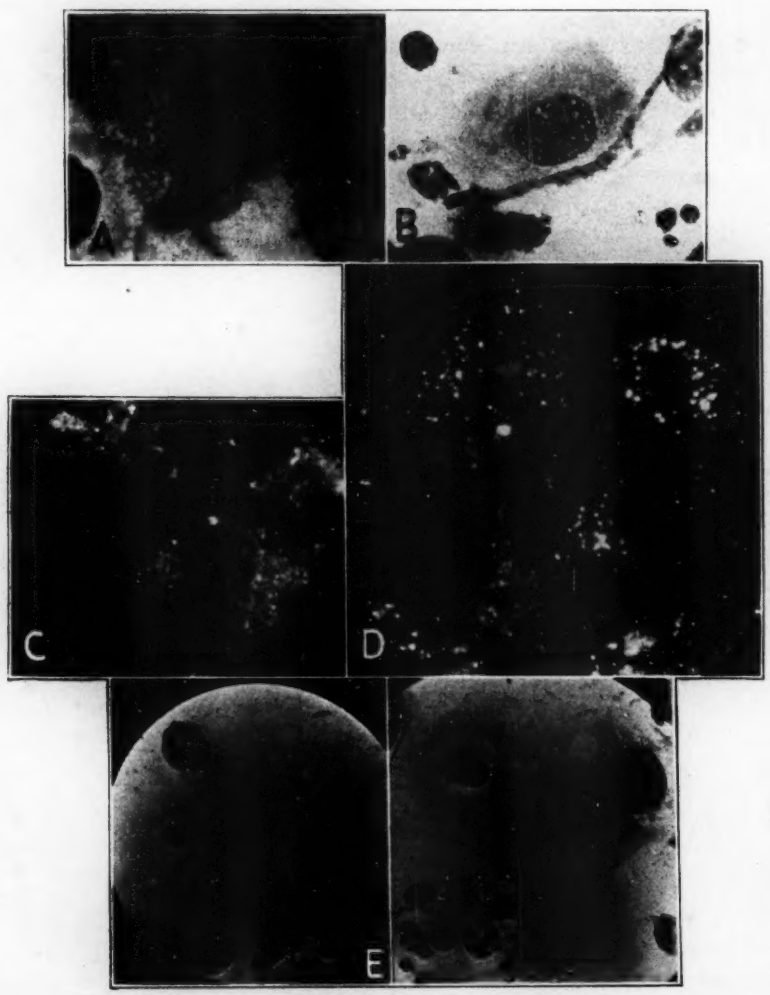

Fig. 1.—*A*, stained mitochondria from normal conjunctiva. *B*, dustlike granules in normal conjunctiva. *C*, dustlike granules in the dark field. *D*, keratin granules in the dark field. *E*, stained keratin granules.

When an elementary inclusion body was seen in a living cell in the bright field, it appeared as an indiscrete granular mass capping the nucleus (fig. 2 *A*). The mass was irregular in outline and appeared to be a part of the cytoplasm; however, by proper adjustment of the transmitted light, the outline could be distinguished. The individual

granules, while indistinct, appeared uniform. When the inclusion was seen in the dark field, it reflected so much light that it appeared homogeneous (fig. 2 *B*) and the individual granules could not be made out with certainty. Such masses differ materially from masses of mitochondria in that the elementary inclusion body is globular while the mitochondria assumes weird, constantly changing, fantastic shapes. According to Rötth,[20] the elementary body is also insoluble in dilute acetic acid.

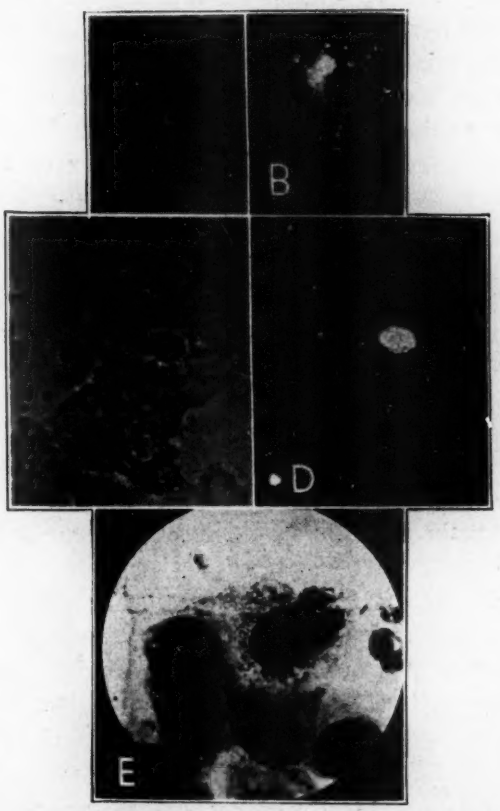

Fig. 2.—*A*, elementary inclusion body in the bright field. *B*, elementary inclusion body in the dark field. *C*, initial inclusion bodies in the bright field. *D*, initial inclusion bodies in the dark field. *E*, scattered elementary bodies.

The initial inclusion body, as seen in the bright field, appeared as a small discrete granular mass (fig. 2 *C*). Such bodies may lie in any position in the cytoplasm. In the dark field the inclusion was composed of brilliantly lighted spherical or oval granules (fig. 2 *D*). Mitochondria or keratin granules in the cytoplasm may be confused with the initial inclusion body when studied in the dark field; however, in my study

20. Rötth, A.: Arch. f. Ophth. **128**:381, 1932.

mitochondria and keratin granules were not seen when the cell was illuminated by direct light, and the initial inclusion bodies were distinct.

The virus of psittacosis is identified easily in dark field preparations.[21] The size of the virus is approximately the same as the measured size of the elementary body of trachoma. In the dark field, the inclusion of psittacosis appears similar to the inclusion of trachoma.

Rice [22] and, later, Thygeson [23] demonstrated that the matrix of the inclusion stains with iodine. Dilute or undilute compound solution of iodine stains the inclusion a deep reddish brown, while the remainder of the cell and other cells stain a pale yellow. In my preparations normal epithelial cells (fig. 1 *C*) when stained with dilute compound solution of iodine became uniformly pale yellow. The mitochondria were not visible in the bright field after staining with iodine but could be seen in the dark field provided the iodine was sufficiently dilute. In the dark field the elementary inclusion body did not reflect the light after staining with iodine, undoubtedly because the stained matrix absorbs light.

At times true elementary inclusion bodies of trachoma were found scattered throughout the cell (fig. 2 *E*). One could confuse these with mitochondria or keratin granules, but on close observation several essential differences were noted. In a cell filled with true elementary bodies the matrix was clear and unstained, while mitochondria and keratin granules lay in a pale blue or pink matrix. Also true elementary bodies were uniform in size and shape and stained uniformly, while the mitochondria and keratin granules varied in size, shape and staining reactions (figs. 1 *A* and 2 *E*).

Whether the etiologic factor of trachoma should be classified as a filtrable virus or as a rickettsia cannot be definitely settled by study of microscopic preparations, but from observations on the trachoma virus it seems to be more closely allied to the former than to the latter.

CONCLUSIONS

1. Mitochondria and keratin granules of normal living conjunctival epithelial cells as seen in the dark field can be stained by the Giemsa method.

2. The inclusion bodies of trachoma and of psittacosis are similar under dark field illumination.

3. The bodies described and photographed by Busacca, Cuénod and Nataf and others undoubtedly represent stained mitochondria and keratin granules rather than rickettsias.

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21. Bland, J. O. W., and Canti, R. G.: J. Path. & Bact. **40**:231, 1935.
22. Rice, C. E.: Am. J. Ophth. **19**:1, 1936.
23. Thygeson, P.: Am. J. Path. **14**:455, 1938.

NAEVUS FLAMMEUS ASSOCIATED WITH GLAUCOMA

REPORT OF A CASE

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The clinical syndrome of naevus flammeus associated with glaucoma has been recognized for many years. It is a relatively rare condition. Schirmer [1] in 1860 was the first to describe this clinical entity, and since then about 75 cases have been reported. O'Brien and Porter [2] in a complete survey of the literature showed that in the majority of the cases the glaucoma was of the infantile type and generally unilateral, the affected eye in many instances being partially or completely blind.

Salus [3] was the first author to show that the glaucoma associated with naevus flammeus need not be congenital but may appear later in life. He cited 2 cases; 1 was that of a woman aged 45 and the other that of a man aged 57.

Usually, the nevus and the glaucoma occur on the corresponding side of the face, but there are exceptions to this rule. Löwenstein [4] reported a case in which naevus flammeus occurred on the left cheek of a woman of 40, who also had a partial glaucomatous excavation of the right disk but with normal tension. The visual acuity and visual field of each eye were normal.

The glaucomatous condition does not always produce partial or complete blindness. In Vögele's case [5] the nevus was on the right side of the face. The disk of the corresponding eye was deeply excavated. The intraocular pressure was increased to 47 mm. of mercury, yet the visual acuity and visual fields were normal.

Read before the Brooklyn Ophthalmological Society, Feb. 17, 1938.

From the Ophthalmologic Service of Dr. W. Moehle, Kings County Hospital.

1. Schirmer, R.: Ein Fall von Telangiektasie, Arch. f. Ophth. **7**:119, 1860.

2. O'Brien, C. S., and Porter, W. C.: Glaucoma and Naevus Flammeus, Arch. Ophth. **9**:715 (May) 1933.

3. Salus, R.: Glaukom und Feuermal, Klin. Monatsbl. f. Augenh. **71**:305, 1923.

4. Löwenstein, A., in discussion on Salus, R.: Glaukom und Feuermal, Klin. Monatsbl. f. Augenh. **70**:540, 1923.

5. Vögele, N.: Glaukom und Naevus flammeus, Klin. Monatsbl. f. Augenh. **81**:393, 1928.

Naevus flammeus and glaucoma may be associated with other bizarre clinical signs. Tyson [6] found right homonymous hemianopia, which was apparently due to a calcified plaque; it was shown roentgenographically to be situated in the region of the left occipital lobe. The tension of the left eye was 45 mm. of mercury. The cupping of the disk was increased, and the blood vessels were pushed to the nasal side. The visual acuity of each eye was 20/20.

That intracranial changes do occur in instances of naevus flammeus has been well established. A history of epileptiform seizures on the side opposite the facial nevus was obtained in 7 of the reported cases. In 5 cases calcified meningeal vessels were demonstrated roentgenographically. Vascular changes were observed in the meninges in three cases in which autopsy was performed. Hemiplegia was noted in 8 of the reported cases on the side opposite the facial nevus.

REPORT OF CASE

D. C., a white man aged 45, came to the outpatient department of the ophthalmologic service on April 20, 1937, complaining of occipital headaches. These headaches began rather insidiously a few months before examination and became progressively worse. They lasted for a number of hours and occasionally for two or three days. Concomitantly with the appearance of these headaches, the patient found it somewhat difficult to read at night. There was no history of halos or of intraocular pain.

His health prior to 1915 had been excellent. While serving with the Russian army, he contracted typhus and pneumonia. In 1919 he had influenza. For the past twelve years he had had pains and aches in both shoulder joints and in the lumbar region. There was no history of a venereal infection. The family history was noncontributory.

The patient was well developed. His heart and lungs were normal. The blood pressure was 162 systolic and 90 diastolic. Otolaryngoscopic examinations revealed nothing more than hypertrophied tonsils.

The blood chemistry and urine were normal. The Wassermann reaction of the blood was negative.

A roentgenogram of the shoulders was normal. A roentgenogram of the lower part of the spine revealed slight hypertrophic changes along the margins of the lower lumbar portion. There was a partial spina bifida occulta of the sacrum. A roentgenogram of the skull revealed the sella turcica to be somewhat shallower than normal. There was no evidence of any calcification of the intracranial vessels.

On the right side of the face, starting at the hair line and extending to the outermost portions of the upper and lower lids of the right eye, was a naevus flammeus. The lids otherwise were normal.

The corneas were clear and measured 12 mm. horizontally. The anterior chambers were normal in depth. The pupils were 3 mm. in diameter and round and regular. They reacted to direct light, consensually and in accommodation. The media were clear. Ophthalmoscopic examination of the right fundus revealed a normal-

6. Tyson, H. H.: Naevus Flammeus of the Face and Globe, Arch. Ophth. **8**:365 (Sept.) 1932.

sized disk, with its margins clearly outlined. The physiologic cup was deep, and the blood vessels were pushed over to the nasal edge. The arteries were somewhat narrowed, and the veins were somewhat fuller than normal. There was no increased tortuousity of the vessels. The macular area, as well as the remainder of the fundus, was normal. The ophthalmoscopic findings in the left fundus were similar to those in the right, except that the physiologic cup was normal in depth and a cilioretinal vessel was present.

Slit lamp examination of the right eye showed that the cornea, anterior chamber and lens were normal. The density of the stroma of the iris appeared to be increased. No blood vessels were seen. The vessels of the bulbar conjunctiva were normal, but the episcleral blood vessels were full, markedly tortuous and convoluted. These changes were particularly marked on the temporal side of the globe.

Slit lamp examination of the left eye gave similar results, but the episcleral blood vessels were not nearly as tortuous and convoluted as those of the right eye.

The visual acuity of each eye was 20/20.

At that time the intraocular tension (Schiötz) was 30 mm. of mercury in each eye. A qualitative perimetric examination revealed a slight concentrically contracted visual form and color fields in each eye, somewhat more marked in the upper and nasal portions of the right eye.

A 1 per cent solution of pilocarpine hydrochloride was prescribed, but the patient did not return for observation. Five months later he returned, again complaining of severe headaches. However, he stated: "When I used the drops, the headaches were not so severe." The visual acuity remained at 20/20. The qualitative perimetric fields were substantially the same as at the previous examination. The intraocular tension of the right eye was 35 mm. of mercury, and that of the left eye, 28 mm. of mercury. The solution of pilocarpine hydrochloride was prescribed again, and the patient was told to return when he had used all of it. When he returned a quantitative perimetric examination revealed a slight concentric contraction of the field, more marked in the upper and nasal quadrants of the right eye. The size of the blindspot of the left eye was normal. The blindspot of the right eye was enlarged laterally and superiorly, forming a beginning Seidel scotoma.

After a lapse of two months, during which time the patient was not using the solution of pilocarpine, he returned, complaining of severe headaches. The intraocular tension of the right eye was now 35 mm. of mercury and that of the left eye, 25 mm. of mercury. Fifty cubic centimeters of a 50 per cent solution of dextrose was administered intravenously, and the intraocular tension was recorded every ten minutes for one and one-half hours. The intraocular tension of the right eye varied between 32 and 38 mm. of mercury; that of the left eye varied between 22 and 28 mm. of mercury.

COMMENT

Naevus flammeus associated with glaucoma occurs in the newborn or the very young and also in much older persons. In any case, partial or complete blindness or some constrictions of the visual fields may occur. The glaucoma is chronic and noninflammatory. Oddly enough, it has been found that various pathologic intracranial changes occur in this condition.

The common clinical ocular signs observed in these glaucomatous eyes may be summarized as follows:

In the conjunctiva or episclera dilated vessels or nevi may be found. In the iris the changes may be heterochromia, increased density of the stroma or dilated blood vessels. In the choroid angiomas or nevi may be seen. In the retina there may be varicosities or tortuous blood vessels, and in the optic disk, increased cupping, alone or combined with partial or complete atrophy.

In the 15 eyes that were examined pathologically it was found that 11 showed angioma of the choroid, 1 showed angiomatous changes in the iris near the filtration angle and 1 showed an irregularity of Schlemm's canal and the scleral spur. In 2 others no changes were observed in the anterior segment or in the choroid. In all the eyes, however, the intraocular capillaries were dilated.

The ocular changes in my patient agree with those just mentioned. His eye showed tortuous and convoluted episcleral vessels, increased density of the stroma of the iris, deep cupping of the optic disk and increased intraocular tension.

This patient, therefore, belongs to the group in whom the glaucoma occurs later in life. He is not totally or even partially blind. His glaucoma is not progressing.

Chronic simple glaucoma can, of course, occur in a patient who happens to have a naevus flammeus. While it is true that it may exist for a little while without inducing subjective symptoms, this time is not of long duration. My patient has been followed for a long period without any apparent aggravation of his symptoms.

The causation of naevus flammeus is unknown. The disease is supposed to be of congenital origin. The cause for the glaucomatous state is also nebulous. There are as many theories for this condition as there are observers. I shall mention but few of them.

Elschnig [7] accounted for the glaucomatous state on the basis of a plethoric condition of the choroidal vessels. This theory, according to him, was supported by the fact that compression of the carotid artery lowered the intraocular pressure.

Yamanaka [8] was of the opinion that there were two causes: (1) a dilatation of the choroidal vessels and an increase in their number, and (2) malformation of the meshwork of the iridocorneal angle with an insufficient outflow of aqueous.

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7. Elschnig, A.: Naevus vasculosus mit gleichseitigem Hydrophthalmus, Ztschr. f. Augenh. **39**:189, 1918.

8. Yamanaka, T.: Naevus Flammeus mit gleichseitigem Glaukom, Klin. Monatsbl. f. Augenh. **78**:372, 1927.

Tyson [6] suggested that the anterior chamber is blocked by a "plasmoid" aqueous resulting from changes in capillary permeability. He used the fluorescein test in his case, and a greenish color of the aqueous of the involved eye was soon apparent, while the aqueous in the normal eye remained clear.

Dunphy [9] and Mehney [10] agreed with Tyson's theory. Dunphy stated that there is no proof that the aqueous in these cases is truly plasmoid, i. e., that its protein content approaches that of the blood. No one, so far as he knew, made any determinations on the aqueous in such cases. Nevertheless, he stated that it is known that any condition which leads to an increased protein content tends to produce an increased formation of aqueous by reducing the difference in the osmotic pressure of the blood and the aqueous. The amount of aqueous formed in any unit of time is therefore increased. He found that the injection of 50 cc. of a 50 per cent solution of dextrose intravenously reduces the intraocular tension of normal eyes by increasing the osmotic pressure of the blood but that it has no effect on the intraocular tension of glaucomatous eyes. According to him, this fact lends support to the theory of abnormal permeability.

Mehney made a chemical analysis of the aqueous in his case and found 0.032 per cent of protein as compared to the normal of 0.02 per cent. The protein content of the blood serum in his case was normal.

CONCLUSION

A case of unilateral naevus flammeus associated with glaucoma of the corresponding eye is presented. This case illustrates (1) that glaucoma need not be of the infantile type but may appear later in life; (2) that blindness, total or partial, need not be associated with this condition, and (3) that Tyson's contention, i. e., that there is a change in the capillary permeability in this disease, comes closest to a true explanation of the observed phenomenon.

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9. Dunphy, E. B.: Glaucoma Accompanying Naevus Flammeus, Am. J. Ophth. **18**:709 (Aug.) 1935.

10. Mehney, G. H.: Naevus Flammeus Associated with Glaucoma, Arch. Ophth. **17**:1018 (June) 1937.

ANGIOID STREAKS

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REPORT OF A CASE OF THE SYNDROME OF GRÖNBLAD AND STRANDBERG [1] (ANGIOID STREAKS AND PSEUDOXANTHOMA ELASTICUM)

History.—A woman aged 48 was admitted to the neurologic ward of the Wilhelmina Hospital on March 26, 1935. During the night of March 23 she noticed a loss of power in her left arm and leg, which had developed insidiously. The next morning there was a disturbance of speech and swallowing. The patient spoke indistinctly and was able to form a few letters only with difficulty. In addition, she noticed that she had difficulty in moving her tongue while speaking. She understood all that was said to her. She complained of a tingling sensation in the affected limbs, more marked in the left leg. "Menstruation" started on March 24 and ended on March 26; the previous week, when the period was due, the patient had also menstruated. This was the first time that this function had been irregular.

Inquiry revealed that for a short time in 1932 the patient's left arm and leg had been weak, at which time there had been a disturbance in speech and swallowing. Neither fever nor chills had occurred while she was at home. During the past five years she noticed that she tired easily and was breathless, especially after climbing stairs, but that she had no difficulty from palpitation. She had no knowledge of any preceding renal disease or of ever having had acute articular rheumatism, St. Vitus' dance or a venereal disease. Questions concerning the internal organs revealed nothing unusual.

The patient came from a healthy family and until her fifth year had never been ill. She had no knowledge of ever having a cutaneous disease. She was married, and her husband was healthy. She had given birth to eight children. At the second confinement twins were born; they were weak and died shortly after birth. The fourth and fifth pregnancies ended in abortions. The patient's father died at the age of 63 (bloody stools and calcified veins). Her mother died at 63 of "old age." The patient knew of no cutaneous disease or ocular trouble existing in the family.

Physical Examination.—The patient looked ill but was compos mentis. She was dyspneic, her face was congested, and the extremities were slightly cyanotic. The pulse rate was 70 per minute, and the pulsations were regular, even, well filled and tense and equal on the two sides. The blood pressure was 210 systolic and 100 diastolic. Respiratory movements were frequent, control of which, though possible, resulted in a limited excursion. The heart was enlarged to the left, the

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Read before the Dutch Ophthalmological Society, Amsterdam, Netherlands, Dec. 13, 1936.

1. From the ophthalmologic (W. P. C. Zeeman), neurologic (B. Brouwer) and pathologic (H. T. Deelman) laboratories of the University of Amsterdam. This case was studied by Drs. Hagedoorn, J. J. G. Prick and E. Sekir, and the report was prepared by Dr. Prick.

apical beat heaving. Auscultation revealed a soft systolic souffle over all the valves. The second aortic sound was louder and more ringing than the second pulmonic sound. On the patient's admission the lungs were free of disease. Examination of the abdomen also gave negative results. The skin of the neck, axillas, chest and abdomen, as well as the flexor surface of the elbows and the folds in the groins, was typical for pseudoxanthoma elasticum. The skin was thickened, lay in folds, felt inelastic and presented violet-tinted, yellowish macular and papular efflorescences. The distribution of the cutaneous condition was symmetric. Examination of the visible mucous membranes revealed nothing abnormal. The fundus of the eye revealed a few angioid streaks and a disk-shaped degeneration of the retina. The papilla nervi optici was surrounded by a gray halo, more marked on the temporal side. Heaps of pigment were seen scattered over the fundus. Neurologic examination revealed left hemiplegia due to involvement of the central nervous system. Active movement of the left arm and leg was practically impossible, whereas the left facial muscles, especially those supplied by the lower branch of the facial nerve, were paretic. The right side of the body also showed signs of cerebral hemiparesis, though less marked, and the muscles supplied by the lingual branch of the right facial nerve were also involved. Surprisingly better was the voluntary innervation of the region supplied by the upper branches of this nerve. The bilateral musculature of the palate and pharynx was under poor control. Both palate arches moved insufficiently with intonation, the left less than the right. Owing to difficulty in swallowing, the patient choked repeatedly. Voluntary movements of the tongue were possible but limited. The tongue deviated from the midline when extended. Turning of the head and lifting of the shoulders occurred in the normal way. On the patient's admission innervation of the muscles of mastication was intact, and no trismus could be established. Ocular movements were normal, and no conjugate deviation was present. Slight nystagmus developed when the patient looked to the right and to the left. Investigation of the special senses brought out the following facts: Sharpness of vision was reduced on each side to ½ and could not be corrected. The visual fields were normal. Hearing, taste and smell were intact. In addition to the disturbance in swallowing, there existed a speech disorder, a dysarthria. Owing to poor articulation, the patient's speech was difficult to understand and in addition had an open nose quality. Spontaneous respiratory movements occurred in a normal way and without any obvious difference between the two sides of the thorax. Sensibility in the region supplied by the trigeminus nerve showed no disorder. Reaction to the vital stimuli was less sensitive in the left arm and leg as well as in the left buttock. Deep sensation was maintained. Coordination of the left arm and leg could not be judged; owing to the marked disturbance of movements, slight ataxia was present in the right arm and leg.

As has been reported, the respiratory movements could be controlled, but only to a limited degree. Therefore no obvious difference between the left and the right side of the thorax could be established. The reflexes on admission were as follows: The pupils reacted to light and in convergence. The corneal and masseteric reflexes were positive. A positive facial reflex was present on the left side. The pharyngeal reflex was, however, absent. No pathologic bulbar reflexes could be elicited. The biceps and triceps reflexes were increased on each side, the left more than the right. The reflexes of Mayer and Leri as well as the abdominal reflex were absent on both sides. The reflexes of Babinski and Chaddock were positive on both sides. A slight hypertonia of the musculature of the arms

and legs existed, more marked on the left. No psychic disturbance could be found. Compulsion laughing and compulsion crying were both absent.

The day after the patient's admission flaccid paralysis of the muscles of mastication developed, and the masseteric reflex had disappeared. During the night of March 28 a curious complication developed in the form of acute bleeding from the gastrointestinal tract. The patient suddenly vomited blood, became pallid and sweated profusely; the pulse beat was small and frequent. Examination of the abdomen revealed no "defense." The gastric region was distended but not tender. Nothing could be found that might lead to a diagnosis of ulcer, carcinoma or hepatic cirrhosis. The following day signs of lobar pneumonia developed. The patient died on April 1.

Laboratory Tests.—The urine contained albumin, hyaline casts and a few clusters of leukocytes. The specific gravity was 1.022. The urea content of the blood serum was 300 mg. per liter (Ambard). The Wassermann and the Sachs-Georgi reaction of the blood were negative. Lumbar puncture was not performed.

The vomitus in addition to blood contained free hydrochloric acid. The feces gave a strongly positive benzidine reaction. The sedimentation rate was 9 mm. in one hour. The blood picture was as follows: hemoglobin (Sahli), 60 per cent (corrected value); leukocytes, 2,200; erythrocytes, 3,900,000; eosinophils, 0; basophils, 0; polymorphonuclears, 4 per cent; segmented polymorphonuclears, 89.5 per cent; lymphocytes, 3.5 per cent, and large monocytes, 3 per cent. On March 29 the hemoglobin content (Sahli) was 48 per cent (corrected value).

Diagnosis.—A clinical diagnosis was made of pseudobulbar paralysis; pseudoxanthoma elasticum, with an associated disease of the fundus; essential hypertension; cardiac hypertrophy and dilatation; hematemesis (cause?), and lobar pneumonia.

GENERAL INTRODUCTION

Grönblad's [1a] statement that pseudoxanthoma elasticum is often associated with angioid streaks (Herman Knapp, 1892) has been repeatedly confirmed. Shortly after the publication of Grönblad, Marchesani and Wirz [2] described the simultaneous occurrence of pseudoxanthoma and angioid streaks.

It should be stated that the simultaneous occurrence of pseudoxanthoma with a disease of the fundus oculi had already been called attention to in a case reported by Hallopeau and Laffitte [3] in 1903. Antonelli, the ophthalmologist who examined the patient, failed, however, to recognize the relation between central chorioretinitis and secondary atrophy of the disk with angioid streaks, which, as figure 1 shows, may have been practically impossible at that time. Hallopeau and Laffitte stated: "Y a-t-il une relation entre ces altérations oculaires

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1a. Grönblad, E.: Angioid Streaks—Pseudoxanthoma Elasticum: Vorläufige Mitteilung, Acta ophth. **7**:329, 1929; Angioid Streaks—Pseudoxanthoma Elasticum: Der Zusammenhang zwischen diesen gleichzeitig auftretenden Augen- und Hautveränderungen, ibid. (supp. 1) **10**:1, 1932.

2. Marchesani, O., and Wirz, F.: Die Pigmentstreifenerkrankung der Netzhaut, Arch. f. Augenh. **104**:522, 1931.

3. Hallopeau and Laffitte: Nouvelle note sur un cas de pseudoxanthome élastique, Ann. de dermat. et syph. **4**:595, 1903.

et le pseudoxanthome? En l'absence d'antécédents et de signes de syphilis ainsi que d'albuminurie et de glycosurie, cette hypothèse est la plus vraisemblable." (Is there a relation between these ocular changes and pseudoxanthoma? In the absence of a history or symptoms of syphilis, such as albuminuria and glycosuria, this hypothesis seems reasonable.) Thus they were the first to detect the relation between pseudoxanthoma and ocular disease.

The fundi of the eyes of this patient could not be studied thoroughly because of her clinical condition; she died a few hours after the ocular examination. It was not possible to make an accurate drawing or a photograph of the fundi. There was marked degeneration of the circumpapillary and the macular region, but it was only just possible to trace a few streaks or lines, which resembled angioid streaks.

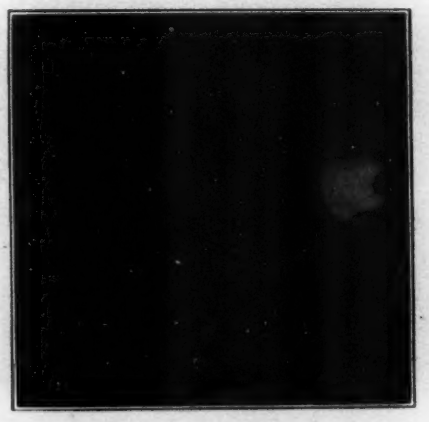

Fig. 1.—Angioid streaks. There is extensive degeneration in the macular and circumpapillary region. The angioid streaks are difficult to trace.

These macular lesions, which usually appear in the later stages of the disease, have often been compared with senile disciform degeneration of the macula (Bonnet [4]).

Figure 1 is a picture of the fundus in a similar case in which the condition was less advanced. The patient had six children who showed no signs of angioid streaks. An eye of one child contained a coloboma of the iris and choroid.

During the last few years several articles dealing with angioid streaks have appeared in the American literature (Dykman,[5] Goedbloed [6] and Benedict [7]). Therefore, the ophthalmoscopic picture does not need introducing. Certain details will be considered later. It will be remembered

4. Bonnet, P.: Evolution des altérations de la macula dans les "stries angioides de la rétine," Arch. d'opht. **52**:225-240, 1935.

(Footnotes continued on next page)

that the streaks may be red; they may also be gray or of varying shades of brown to almost black. The edges more often have the appearance of torn paper than the smooth straight or curved boundaries of a wall of a vessel. Figures 2, 3, 6 and 7 demonstrate the variability of the fundus picture of angioid streaks.

In the cases mentioned in this paper the clinical and histologic diagnosis of pseudoxanthoma was made or confirmed by Dr. W. L. L. Carol, professor of dermatology at the University of Amsterdam.

HISTOLOGIC PICTURE OF ANGIOID STREAKS AS DESCRIBED IN THE LITERATURE

The eye described by Lister [8] was seriously damaged and cannot be accepted as one affected with angioid streaks. Magitot [9] gave a histologic

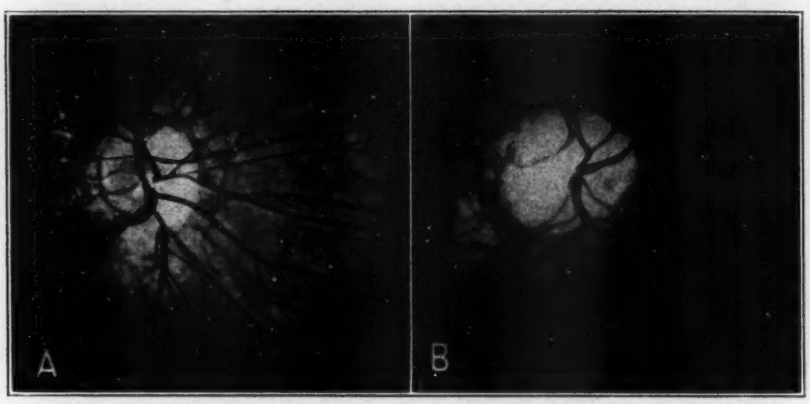

Fig. 2.—Angioid streaks. In *A* the streaks are readily seen. There is no secondary macular degeneration. Note the gray shade of the fundus and the absence of choroidal vessels. Confusion of the streaks with choroidal vessels is impossible. In *B* the streaks are readily seen, but confusion with choroidal vessels is possible.

description of Siegrist's [10] pigmented streaks in arteriosclerosis of the choroid. The changes observed by Verhoeff [11] in an eye damaged by

5. Dykman, A. B.: Angioid Streaks of the Retina: A Report Concerning Two Cases Associated with Pseudoxanthoma Elasticum, Arch. Ophth. **11**:283 (Feb.) 1934.

6. Goedbloed, J.: Syndrome of Groenblad and Strandberg: Angioid Streaks in Fundus Oculi, Associated with Pseudoxanthoma Elasticum, Arch. Ophth. **19**: 1 (Jan.) 1938.

7. Benedict, W. L.: The Pathology of Angioid Streaks in the Fundus Oculi, J. A. M. A. **109**:473 (Aug. 14) 1937.

8. Lister, W. T.: Angioid Streaks of the Retina, Ophth. Rev. **22**:151, 1903.

9. Magitot, A.: Pigmentation angioide de la rétine, Ann. d'ocul. **145**:2, 1911.

(Footnotes continued on next page)

iritis, glaucoma and iridectomy, with loss of vitreous, cannot, as Franceschetti and Roulet [12] concluded, be accepted as typical for the anatomic substrate of angioid streaks; ophthalmoscopic examination was impossible in this case. In the other eye of Verhoeff's patient a gray zone surrounding the optic disk was seen, from which there extended two white streaks. Over a portion of the fundus of the enucleated eye, dark "angioid streaks" were seen macroscopically, which on microscopic examination were revealed as being parts of the inner layers of the choroid, thrown into ridges by a cicatricial contraction of fibrous tissue, the latter having replaced the deeper layers. Such a histologic picture does not fit in with the clinical findings; moreover, the diagnosis of true angioid streaks in the other eye cannot be considered as definitely proved. Wilmer [13] reported a case in which investigation was incomplete. Benedict [7] in a recent paper reported that he was unable to find any specific histologic lesion. Probably this was due to the way in which the sections were made. Law [13a] identified angioid streaks with the retinal folds he found in his interesting case (with gastric hemorrhage).

It may be concluded that a histologic description of angioid streaks is still lacking, though on the basis of ophthalmoscopic studies it seems probable that the primary site of the condition must be found in Bruch's membrane (Grönblad). Böck's [13b] observations are in accordance with my findings in 1936.

DIFFERENTIAL DIAGNOSIS

Angioid streaks, no matter how varied in shape and color they may be, are generally so typical that but few conditions can give rise to difficulties in differential diagnosis. Confusion with choroidal vessels (fig. 4) is not likely to occur if the aspect of angioid streaks is familiar to the observer. Siegrist's pigmented streaks in arteriosclerosis of the choroid may simulate angioid streaks, but their rough, irregular, darkly

10. Siegrist, A.: Beitrag zur Kenntnis der Arteriosklerose der Augengefässe, Internat. Ophth. Kong., Utrecht, 1899, p. 131.

11. Verhoeff, F. H.: The Nature and Pathogenesis of Angioid Streaks in the Ocular Fundus, Tr. Sect. Ophth., A. M. A., 1928, p. 243.

12. Franceschetti, A., and Roulet, E. L.: Le syndrome de Groenblad et Strandberg (stries angioïdes de la rétine et pseudoxanthome élastique) et ses rapports avec les affections du mésenchyme, Arch. d'opht. **53**:401, 1936.

13. Wilmer, W. H.: Angioid Streaks of the Choroid, in Atlas Fundus Oculi, New York, The Macmillan Company, 1934, fig. 92; cited by Franceschetti and Roulet.[12]

13a. Law, F. W.: A Contribution to the Pathology of Angioid Streaks, Tr. Ophth. Soc. U. Kingdom **58**:191, 1938.

13b. Böck, J.: Zur Klinik und Anatomie der gefässähnlichen Streifen im Augenhintergrund, Ztschr. f. Augenh. **95**:1, 1938. His paper appeared after this report had been submitted for publication, so that it cannot be discussed as it deserves.

pigmented aspect is seldom observed in angioid streaks and never over the entire course of the streaks. The condition in Ejler Holm's [14] cases, described as angioid streaks, was of this type.

Striate retinitis must also be borne in mind. Under this heading various conditions have been described, even angioid streaks. Striate retinitis is described as following detachment of the retina. The streaks are not so sharply marked off, are not red and lack the peculiar torn-paper aspect of angioid streaks; there are generally other rests of detachment present (pigmentation) or at least a history of detachment. The term striate retinitis is found in "Kurzes Handbuch der Ophthalmologie" but not in Parson's textbook, "Pathology of the Eye." Rönne [15] reported finding a strand of connective tissue between the retina and the choroid in a case of striate retinitis; other authors have expressed the belief

Figure 3

Figure 4

Fig. 3.—Angioid streaks. Smaller streaks resembling a lake district are seen bordering the disk.

Fig. 4.—Myopic fundus. The choroidal vessels simulate angioid streaks.

that the strands are ridges in the choroid. Striae, typical of detachment, have been described by Leber.[16] Figure 5 probably represents the anatomic substrate of such a stria, which is entirely different from the pigmented streaks, marking off an old detachment. It was found in one of the eyes described by Van der Meer.[17] In addition,

14. Holm, E.: On the Site of the Angioid Streaks in the Fundus Oculi, Acta ophth. **2**:152, 1924; Pigmented Chorioidal Vessels, ibid. **5**:188, 1927.

15. Rönne, H.: Zur Anatomie der Streifenbildung nach Netzhautablösung, Arch. f. Ophth. **75**:284, 1910.

16. Leber, in von Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Engelmann, 1916, vol. 7, p. 1442, fig. 230.

17. Van der Meer, B. C. J.: Over de operatieve behandeling van netvlies-loslating, Maastricht, Netherlands, Stols, 1935.

other varieties of streaklike pigmentations and demarcations may occur in cases of older retinal detachment.

The whitish "atrophic" appearance of the circumpapillary region may dominate the picture in cases of angioid streaks (fig. 6), the streaks being

Fig. 5.—Retinitis striata; cross section through the retinal stria in a case of retinal detachment. Van Gieson's stain; × 122.

Fig. 6.—Angioid streaks, with involvement of the circumpapillary region. The streaks are less generalized but are readily seen.

visible only on careful examination. (They were even difficult to trace in the fundi showing figure 7. In a similar case but one in which the condition was less advanced the diagnosis remained doubtful, since the cutaneous condition was absent and definite angioid streaks could not be

traced [fig. 8]). In myopia the circumpapillary region may also be white and irregularly pigmented, but the sharp line of demarcation of the atrophic areas at the posterior pole is different from the gradual fading of the prominent areas of degeneration ("pseudotumor"), as is seen in angioid streaks and in advanced stages of Junius and Kuhnt's

Fig. 7.—Angioid streaks, in a case of pseudoxanthoma of the skin with grayish involvement of the circumpapillary region. A large hemorrhage is present in the macula. The diagnosis was difficult and the angioid streaks are difficult to trace.

Fig. 8.—No diagnosis was made. There is circumpapillary involvement. The fundus is dark, the streaks are not typical and there is no pseudoxanthoma. The white beam under the disk is a reflection from the nerve layer of the retina.

disease. The presence of a myopic refraction cannot be taken into consideration, since angioid streaks may appear in a patient affected with myopia. Arteriosclerosis of the choroid, as a more or less independent choroidal disease, though generally affecting the posterior pole, may also involve the circumpapillary region (halo senilis). Since angioid

streaks have been mistaken for choroidal vessels, confusion is possible, but the characteristic course of preserved and sclerotic choroidal vessels will generally leave little doubt as to the correct diagnosis.

The identity of the early stages and varieties of angioid streaks may be difficult to establish. Tapetoretinal degeneration (Zeeman), also a choroidal disease, without any trace of angioid streaks (Batten) has been described. These anomalies will be dealt with more extensively later.

Since angioid streaks as such do not give rise to clinical symptoms, the patient is generally seen only if the macular region becomes involved. The whole group of possible macular conditions might therefore be mentioned as being of interest from the point of view of differential diagnosis. Since a serous exudate may be the first sign, angioneurotic, allergic and angiospastic conditions, macular degeneration and the first stage of Kuhnt's retinitis centralis atrophicans should be mentioned. The postedematous stage must be differentiated from macular degeneration, congenital anomalies, tumors and postinflammatory and traumatic conditions. However, a careful examination of the fundus and skin will nearly always lead to the correct diagnosis. Among these diseases, disciform degeneration is the most important and related. In both disciform macular degeneration (Junius and Kuhnt) and ordinary senile macular degeneration the serious changes around the disk, which are so characteristic in many cases of advanced angioid streaks, are often lacking. Angioid streaks is principally a circumpapillary disease, whereas disciform macular degeneration is a submacular disease.

This ophthalmoscopically related condition of disciform degeneration (fig. 9) of the macula (*scheibenförmige Entartung der Netzhautmitte* [Junius and Kuhnt [18]]; *rétinite exsudative maculaire sénile* [Coppez and Danis [19]]) has been carefully studied histologically. In this disease a fibrous tissue develops between Bruch's membrane and the retina, appearing first under the pigmented epithelium. That the disease develops secondary to degeneration of Bruch's membrane, which, it is said, has a physiologic importance, was accepted as an established fact (Behr [20]; Rintelen [21]). Recently, however, on the basis of a careful study of the histologic picture in 3 private cases and a survey of the

18. Junius, P., und Kuhnt, H.: Die scheibenförmige Entartung der Netzhautmitte, Berlin, S. Karger, 1926.

19. Coppez, H., and Danis, M.: Rétinite exsudative maculaire sénile et rétinite circinée, Arch. d'opht. **43**:461, 1926.

20. Behr, C.: Ein weiterer Beitrag zur Anatomie und Pathogenese der scheibenförmigen Degeneration des hinteren Augenpols, Ztschr. f. Augenh. **75**: 216, 1931.

21. Rintelen, F.: Zur Histogenese des senilen submaculären Pseudotumors, Klin. Monatsbl. f. Augenh. **97**:673, 1936.

literature, covering 129 eyes, Verhoeff and Grossman [22] supported the view that the condition is primarily due to "some disturbance in the choriocapillaris, probably localized angiosclerosis." From the diseased choroid a hemorrhagic extravasate may settle between the pigmented epithelium and Bruch's membrane and undergo organization. This process is considered by Verhoeff and Grossman to be the "usual, if not the only, pathogenesis of this disease." Davenport [23] in his paper on senile macular exudative retinitis gave a clinical description of cases in which there was a large hemorrhage behind the macula. In the report of their third case Verhoeff and Grossman mentioned the presence of a serous exudate between the choroid and the retina, which is in agreement with Behr's findings; the latter expressed the belief that this exudate represents the first stage of the disease. Verhoeff and Grossman accepted this point of view as significant for cases of the juvenile type only and cases of serous retinitis secondary to "vascular disturbance dependent on some cause or causes yet to be determined."

Serous disciform chorioretinitis of the macula has been described by Batten,[24] Oguchi,[25] Kitahara [26] and Rauh [27] as a circumscribed macular detachment with no tendency to further development of a dialysis of the retina. Zeeman [28] demonstrated this condition in 7 patients; in 1 it followed iridectomy and in 1 there was a pit in the optic disk. Similar observations have been reported in cases of angioid streaks; recently Goedbloed described such a case. Though serous detachment of macula occurs in disciform degeneration, this simple fact is not sufficient reason for identifying this disease with retinitis disciformis. The diagnosis of juvenile disciform degeneration should be made only with great caution.

Typical for an earlier period of life is Coats's disease, retinitis exsudativa externa. In Coats's disease, Verhoeff, who personally made a histologic examination in several cases, also found new tissue present but not developing primarily beneath the pigmented epithelium. In the

22. Verhoeff, F. H., and Grossman, H. P.: Pathogenesis of Disciform Degeneration of the Macula, Arch. Ophth. **18**:561 (Oct.) 1937.

23. Davenport, R. C., cited by Rea, R. L.: Neuro-Ophthalmology, St. Louis, C. V. Mosby Company, 1938, p. 154.

24. Batten, R. W.: Macular Disease with Special Reference to Acute Primary Macular Disease, Tr. Ophth. Soc. U. Kingdom **41**:411, 1921.

25. Oguchi, C.: Eine besondere Form von Chorioretinitis centralis nebst Bemerkungen über nachbildartiges Skotom, Arch. f. Ophth. **110**:25, 1923.

26. Kitahara, S.: Ueber klinische Beobachtungen die der in Japan häufig vorkommenden Chorioretinitis centralis serosa, Klin. Monatsbl. f. Augenh. **97**: 345, 1936.

27. Rauh: Ueber seltene Erkrankungen der Netzhautmitte, Ztschr. f. Augenh. **60**:209, 1926.

28. Zeeman, W. P. C.: Retinitis disciformis serosa, Nederl. tijdschr. v. geneesk. **81**:2995, 1937.

early stages a large amount of fibrin and hematogenous pigment is present. In the later stages cholesterol crystals surrounded by giant cells may be numerous. Verhoeff concluded that the origin of Coats's disease seems to be primarily retinal; that of Junius and Kuhnt's disease, primarily choroidal. In addition to these histologic differences, clinical anomalies of the vessels of the retina (fig. 10), convolutions of vessels and aneurysms are frequently seen in Coats's disease. Further, the condition is nearly always unilateral, whereas disciform degeneration is bilateral.

Though circinate retinitis has been reported in association with angioid streaks (also in a case of choroidal disease [Batten] in the brother of a patient with angioid streaks), this condition has to be considered as secondary to lesions in the deeper layers or to a related disease of

Figure 9

Figure 10

Fig. 9.—Disciform degeneration of the macula (Junius and Kuhnt). There is absence of angioid streaks and of circumpapillary involvement. The fundus is dark.

Fig. 10.—Coats's disease. Anomalies of the vessels are seen.

the retinal vessels (Morax[29]). This choroidal disease, as described by Batten,[30] will be discussed later.

TECHNIC OF HISTOLOGIC STUDY

The two eyes used for histologic study (1335 and 1335a) were enucleated post mortem; a small cap was cut off above and below and was preserved in a solution of formaldehyde. Serial pyroxylin sections of 15 microns were made and stained according to various methods or were preserved in alcohol with the caps. In the future it would be better to fix the specimens of one eye in a neutral solution

29. Morax, V.: Etude anatomo-pathologique d'un cas de dégénérescence circinée de la rétine, Ann. d'ocul. **163**:801, 1926.

30. Batten, D.: Angioid Streaks and Their Relation to a Form of Central Chorioidal Disease, Brit. J. Ophth. **15**:279, 1931.

of formaldehyde, since ordinary (acid) solution of formaldehyde may contain formic acid, which may cause small amounts of calcium and iron to disappear from the sections due to the formation of water-soluble calcium formate. In daylight formic acid develops continuously from solution of formaldehyde, so that the specimen should be kept in the dark. In addition, one eye should be preserved without the use of alcohol, so as to avoid solution of fatty material. Thus frozen sections should be made, either with or without embedding in gelatin.

GENERAL SURVEY OF HISTOLOGIC STUDY

The anomalies found in the two eyes were nearly identical, so that they will not be described separately. The eyes showed serious alterations around the disk, culminating in the macular region. In addition, an almost completely atrophic region of the retina was found at the nasal side of eye 1335a. Both of these areas in eye 1335a were easily located macroscopically, since here the elsewhere artificially detached retina was still attached to the underlying tissue. The retina was more adherent in eye 1335. In studying the sections stained with hematoxylin and eosin one was struck by the confusing variety of pathologic changes; there was, however, one constant and dominating feature in both eyes: the pathologic condition of Bruch's membrane (fig. 11 *A*). In a normal eye stained similarly the membrane was not visible, at least not with low magnification, whereas in these sections it seemed to be considerably thickened and was overstained with hematoxylin. Consequently, it was easily followed from the posterior pole to the equator, whereas toward the periphery it became less distinct. Besides the thickening and excessive basophilia, the membrane behind the equator showed a great number of defects, gathered especially around the disk. In the macular region the membrane was missing over considerable distances. Under high magnification the margins of most of the defects were as clearcut as though done with a knife (fig. 11 *B*). Therefore, it may be concluded that the defects were true ruptures of the membrane. The parts of the membrane bordering a defect showed no tendency to curl as does Descemet's membrane.

BRUCH'S MEMBRANE

Reconstruction of Defects in Bruch's Membrane.—A sufficiently accurate reconstruction of a plane view of Bruch's membrane in the nasal region adjacent to the disk was possible. On a projected picture of a section two parallel lines were drawn, one on each side of the optic nerve; a third line was constructed between these lines. A fourth line, nearly perpendicular to the first three, connected the end of Bruch's membrane to both sides of the optic nerve. It was assumed that the crossing point of lines 3 and 4 belonged to a line running perpendicular to the plane of the section (line 5). The distances between the edges

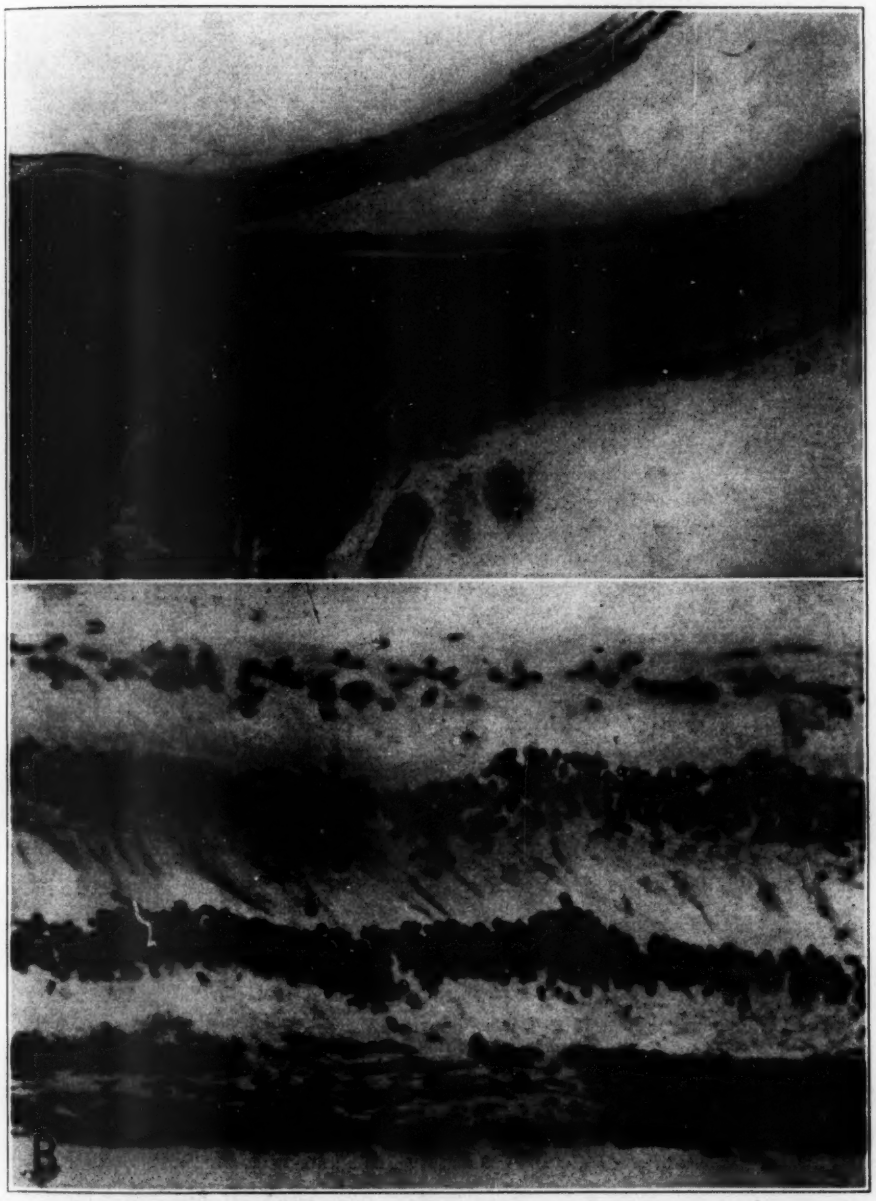

Fig. 11.—*A*, angioid streaks. Hematoxylin and eosin stain; × 40. The retina is detached, and Bruch's layer is thickened and broken. *B*, angioid streaks. Hematoxylin and eosin stain; × 225. Note the clearcut edges of rupture in Bruch's layer.

of several ruptures to the corresponding crossing points were measured in a number of subsequent sections and transcribed to a schema of parallel lines, so spaced as to represent adequately the subsequent sections. It is true that line 5 is not in reality a straight line, but the including of many ruptures in these estimations acted as a valuable correction. By comparing the transcribed dots of two adjacent lines in the reconstruction schema, it became immediately obvious that a slight correction, either to the right or to the left, was necessary. Figure 12 demonstrates the similarity of the reconstructed defects to the clinical picture of angioid streaks. They are different from ruptures of Bruch's membrane in cases of high myopia.

Extent of Involvement of Bruch's Membrane.—In the sections studied the thickening and basophilia of the membrane proved to be constant and complete in the region behind the equator. In the macular region the membrane was sometimes atrophic. Apparently normal areas, which

Fig. 12.—Angioid streaks. Reconstruction of ruptures in Bruch's layer from the sections. The dotted line represents the projected circumference of the optic nerve.

did not stain with hematoxylin, appeared toward the periphery. The transition to these areas was short, though not abrupt. Thus normal areas alternated with thickened and overstained areas over the entire periphery till the pars plana was reached. It was practically impossible to make a plane view reconstruction of the diseased parts in this region, except for two areas at the extreme periphery, where an ordinary cystic degeneration of the retina served as a landmark in localizing the diseased portion (fig. 13), so that a reasonably accurate reconstruction was possible. Thus it could be proved that the two affected areas were small, nearly round islands of diseased membrane.

The caps cut from the eyes before embedding included a part of the choroid.

An effort to study Bruch's layer in plane view in small pieces of depigmented choroid, stained with orcein and made translucent after the procedure that was employed by Spalteholz, was made. Knowledge beforehand that this degeneration existed made it possible to trace

the affected areas, in which the fibers were somewhat coarser, but the results were disappointing; it was not possible to draw any conclusions whatever from these pictures alone. Perhaps this was due to the fact that the material available for these investigations was limited. Other pieces of choroid were stained with hematoxylin. The irregular distribution of the diseased areas could be observed. However, it was impossible to make a clear photograph, owing to the heavily pigmented epithelium on the one side and of the stained choroid on the scleral side. Therefore, a drawing was made to demonstrate these areas (fig. 14). For better results it seemed reasonable to depigment the specimen before staining with hematoxylin. This procedure spoiled the basophilia of Bruch's membrane, so that the results were unsatisfactory. For this

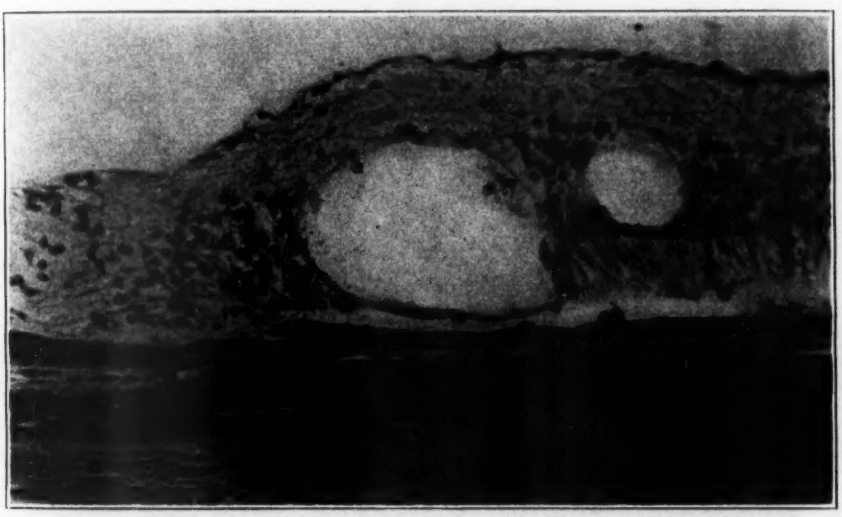

Fig. 13.—Angioid streaks. Hematoxylin and eosin stain; × 225. Cystic degeneration of the peripheral portion of the retina is present. Bruch's layer is scarcely visible and is thickened in the region under the smaller cyst.

reason figure 14 is of a hematoxylin-stained section which has not been depigmented.

The broken ends of the membrane and the membrane itself bordering the ruptures were straight, not undulated, so that the degeneration seemed to be associated with a process of shortening, which, however, as could be seen from the reconstruction, was not as marked as might appear from a study of sections. A detailed study of Bruch's membrane requires knowledge of its normal structure.

Normal Histologic Structure of Bruch's Membrane.—Wolfrum described Bruch's membrane as consisting of two layers, an outer collagenous elastic layer, measuring about 0.5 micron, and a much thinner

inner layer of no measurable thickness, less than 0.25 micron, the latter being the basal layer of the pigmented epithelium of the retina.

Wolfrum [31] (and former authors) described the very delicate elastic fibers of the elastic membrane as often making hairpin turns to enter the choriocapillaris, where they become considerably thickened. In eye

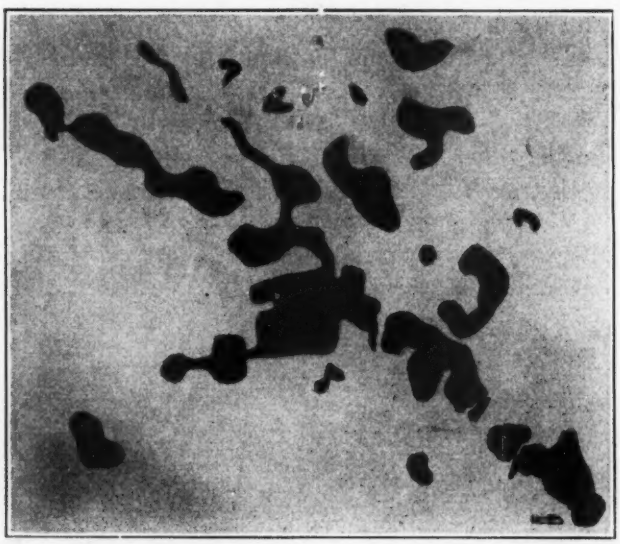

Fig. 14.—Drawing showing areas of degeneration in Bruch's layer. A piece of choroid was stained in toto with hematoxylin. There was a macular staining of Bruch's layer which could not be photographed, since the pigmented epithelium veiled the picture. Depigmentation spoiled the hematoxylin stain of Bruch's layer.

Fig. 15.—Hypertension. Hematoxylin and eosin stain; × 950. Septums in the choriocapillary layer are inseparably connected with Bruch's layer.

P. A. 1293 (a case of hypertension) the relation of Bruch's layer to the septums in the choriocapillaris was pathologically exaggerated (fig. 15); according to Wolfrum this layer must be considered not as a membrane,

31. Wolfrum, M.: Beiträge zur Anatomie und Histologie der Aderhaut beim Menschen und bei höheren Wirbeltieren, Arch. f. Ophth. **67**:307, 1908.

but as the extreme inner region of the elastic system of the choroid. These statements could be confirmed in sections of sarcomatous eyes. The outer layer is not an elastic "membrane" but a network of tiny elastic and collagenous fibers. Whether it functions as a membrane cannot be judged. It should be called "Bruch's layer." There can be no historical objection to connecting Bruch's name with this layer, since this author observed the thick posterior layer only and was not acquainted with the minute histologic structure of the region. (The original article [32] was not available to me.) There exists a potential space between the inner and the outer layer, and normally they are never adherent, so that leukocytes may penetrate between them. The inner layer is always adherent to the pigmented epithelium. It should be called the basal membrane of the pigmented epithelium. The name Bruch's membrane should be maintained in all those instances in which a separate study of the two layers has proved impossible. This is the case in nearly every reported study in which a description of the condition of Bruch's membrane is given.

In the following discussion of Bruch's membrane consideration will be given to whether the membrane has degenerated as a whole or whether only one of the two layers has been affected.

Bruch's Membrane in Pyroxylin Sections.—The thickening and basophilia in the sections stained with hematoxylin have been described (fig. 17 *C*). Since thickening, basophilia and brittleness of the elastic tissue are also found in pseudoxanthoma, these conditions might be considered identical, a supposition which raised the theoretic question of a disease of the elastic system as a whole. Such a satisfactory explanation was apparently upset, however, by evidence found in sections stained with orcein, a dye staining electively elastic fibers; such sections were compared with the normal membrane of a sarcomatous eye. At the posterior pole the membrane stained well but was not thicker than normal (fig. 16 *A*). Toward the periphery it became somewhat thicker, without, however, decidedly differing from the membrane of the sarcomatous eye. It was impossible to recognize the islands of degeneration with this stain. In front of the thin elastic layer a thick, homogeneous, faintly staining layer was seen, which by comparison with the sections stained with hematoxylin could be interpreted as being the thickened basal membrane of the pigmented epithelium (fig. 16 *A*). Combined staining with hematoxylin and orcein did not furnish satisfactory results, since orcein interfered with the hematoxylin. At first it was concluded that the basal membrane was thickened and pathologic, Bruch's layer being fairly

32. Bruch, C.: Untersuchungen zur Kenntnis des körnigen Pigments der Wirbelthiere in physiologischer und pathologischer Hinsicht, Zurich, Meyer u. Zeller, 1844.

Fig. 16.—*A*, angioid streaks. Orcein stain; × 810. In the upper part of *A* Bruch's layer is thin. Apparently anterior to it is a thick amorphous layer. In the lower part are seen the third stage of degeneration of the choroidal vessel and atrophy of the elastic tissue. *B*, angioid streaks. Hematoxylin and eosin stain; × 580. Bruch's layer in the macular region is homogeneous and crisp.

normal. But on further study, especially of peripheral and damaged sections stained with hematoxylin, it was revealed that the membrane gave a false impression of being thickened. One of the sections in which an apparently thick, darkly stained membrane was seen was studied further under powerful blue filtered illumination. The membrane was then seen as being delicately stained and translucent. Its cut surface could be easily distinguished from the shadow-like appearance of that part of the membrane which was not in focus. By bringing all parts of the membrane in and out of focus, there remained not the least doubt that whereas under ordinary light the membrane stained with hematoxylin appeared thick, it was in reality just as thin as that seen in the sections considerably less intensely stained with orcein. It may be concluded that the apparent considerable thickening of the membrane in sections stained with hematoxylin was, for the greater part, an optical illusion, the overstaining making it impossible to distinguish the plane of section from the shadow of that part of the membrane out of focus. The membrane at the degenerated areas in the periphery did indeed seem to be somewhat thickened, whereas at the posterior pole it was decidedly thinner than normal, so thin in fact that at the macular region it resembled a thin sheet of crisp old paint which had peeled off (fig. 16 *B*). It may be concluded that the onset of degeneration as seen at the periphery causes a slight thickening of Bruch's membrane, which, as the degeneration proceeds, becomes thinner, till at the posterior pole it may become atrophic. For a more detailed study it is necessary to consider the behavior of the pigmented epithelium over the diseased membrane.

Pigmented Epithelium and Involvement of Bruch's Membrane.—Since the pigmented cells are inseparably connected with their basal layer, the so-called inner layer of Bruch's membrane, they have to be included in a study of this membrane.

It is interesting to consider a possible relation between the development of an amorphous layer, probably an exudate, and the degenerated areas at the periphery of Bruch's layer, since these exudates occurred at the site of the degeneration (fig. 17 *A* and *B*). That the pigmented epithelium was as a whole pushed aside by this exudate points to the fact that its basal membrane must have been unimpaired. It did not stain with hematoxylin as did Bruch's layer, from which it was separated by the exudate. Therefore, it may be concluded that the basal membrane of the pigmented epithelium does not share in the degeneration of Bruch's layer, at least not in the feature of becoming excessively basophilic.

Evidently the degeneration of Bruch's layer allows a passage of fluid from the choriocapillaris, or it induces the pigmented epithelium

to secrete a subepithelial mass, in the manner described by Koyanagi [33] in hypertension. The latter supposition is the less probable since as degeneration proceeds, which is the case as one passes from the periphery toward the equator, the exudate is missing and the pigmented epithelium lies directly on the continuously degenerated Bruch's layer (fig. 17 *C*). Furthermore, the secretory activity of the pigmented epithelium described by this Japanese author is considerably different from that considered here. As one approaches the posterior pole, ruptures bridged by apparently unaltered pigmented epithelium may be seen—a fact which confirms the supposition that the basal membrane behaves independently and does not share in the degeneration. Other

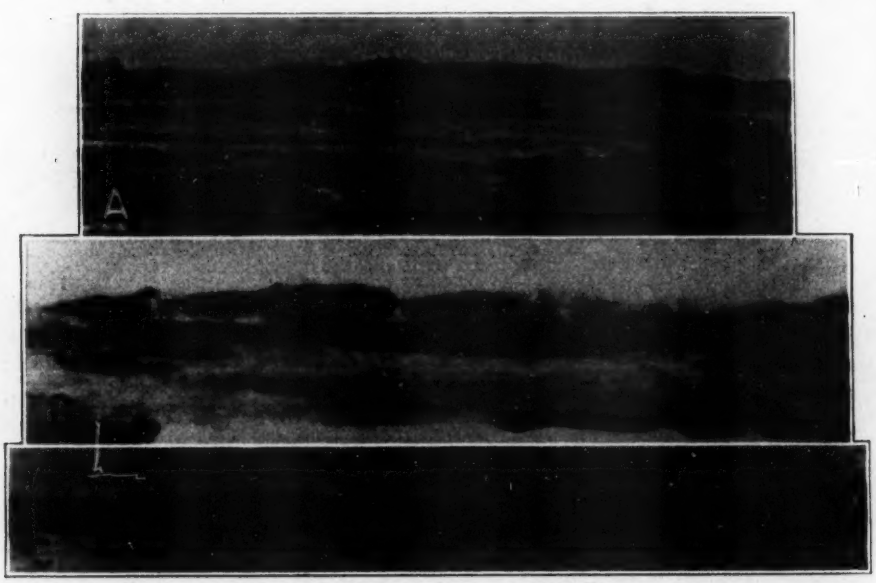

Fig. 17.—*A* and *B*, angioid streaks; peripheral region. *A*, pyroxylin section. Hematoxylin and eosin stain; × 590. The exudate at the site of the localized degeneration of Bruch's layer is pushing off the pigmented epithelium. *B*, paraffin section. Hematoxylin and eosin; × 1,050. Note the isolated degeneration of fibers in Bruch's layer. There is an exudate or a homogeneous layer at the site of the degeneration between the pigmented epithelium and Bruch's layer. *C*, angioid streaks; equatorial region. Hematoxylin and eosin stain; × 480. Bruch's layer is considerably "thickened." The pigmented epithelium is apparently fairly normal and is seen lying directly on Bruch's layer.

serious changes which occur nearer the posterior pole will be described later.

33. Koyanagi, Y., and Kinukawa, C.: Gleichartige Veränderungen des retinalen Pigmentepithels und des renalen Tubulusepithels bei verschiedenen Vergiftungen (Beiträge zur Pathogenese der Rétinitis albuminurica), Arch. f. Ophth. **137**:261, 1937.

Minute Anatomy of the Degeneration of Bruch's Layer.— Even in the sections embedded in pyroxylin and stained with orcein, the individual fibers still could be easily demonstrated (fig. 18 *A*) if the membrane were twisted. The fibers are more delicate and regular in a normal

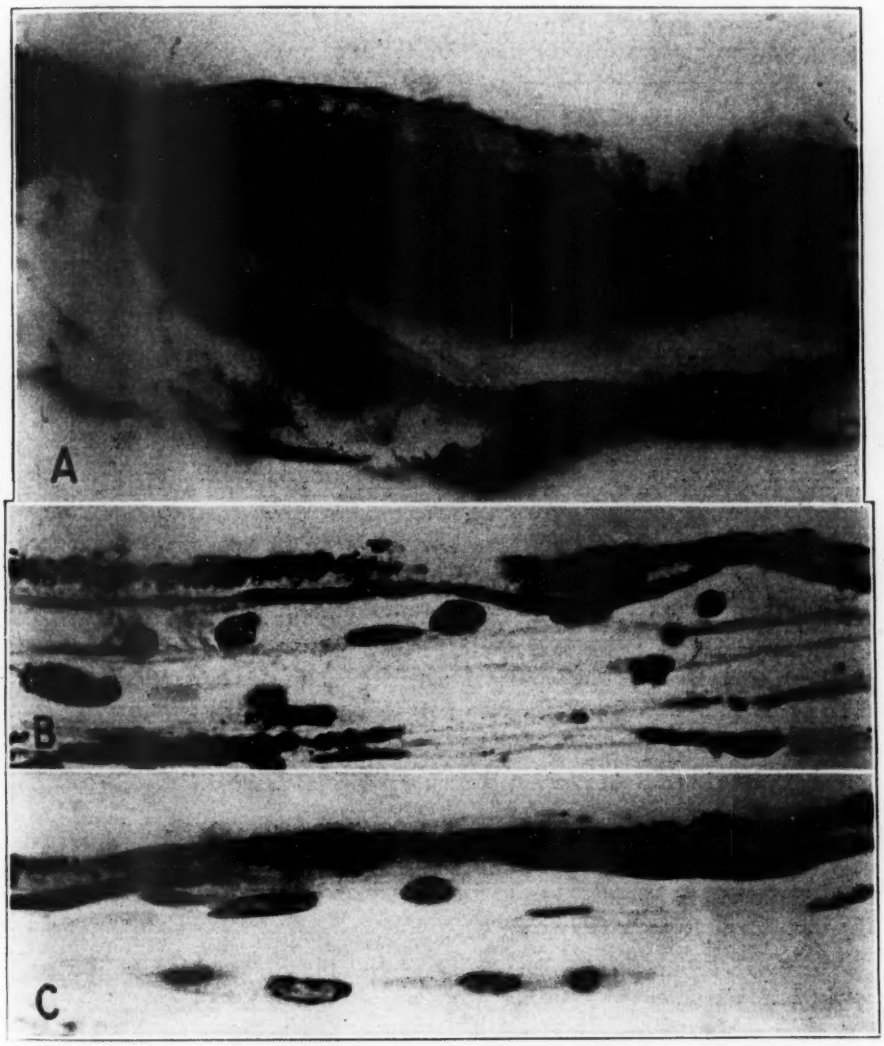

Fig. 18.—*A*, angioid streaks. Damaged pyroxylin section. Orcein stain; × 800. Bruch's layer is twisted. Individual fibers are traceable but irregular and coarser. The fibrillar character of the membrane is still maintained. *B* and *C*, angioid streaks. Paraffin sections. Hematoxylin and eosin stain; × 1,050. There is degeneration of individual fibers at the borders of the islands of complete degeneration.

eye (fig. 43). The aforementioned caps which were cut from the eyes included a part of the choroid; this was carefully separated from the sclera and paraffin sections made of it. In the sections stained with hematoxylin it could be definitely proved that basophilia of Bruch's layer does not at the onset occur as a whole but that isolated fibers within the layer degenerate individually. The fibers seen in figure 18 *B* and *C*, though cut, are still viewed partly in plane view, owing to the fact that the thickness of the sections is 6 microns and the thickness of Bruch's layer, from 0.5 to 1 micron. Degenerated fibers, though occasionally seen in an apparently normal part of the layer, are generally observed in the neighborhood of more completely degenerated regions. It appears that the layer in the more severely affected areas loses its fibrillar character. Becoming more membranous, it stains more evenly, showing only a faint network of more or less sharply marked off degenerated fibers. The disappearance of the individual fibers was excellently demonstrated in the pyroxylin sections (fig. 19 *A*), if the layer was twisted and the pigmented epithelium torn off. Finally, no trace of individual fibers is left (fig. 16 *B*). The affinity of Bruch's layer for orcein is maintained until complete atrophy develops (fig. 19 *B*).

Special attention was paid to the behavior of the elastic fiber as it dips into the choroid. As a rule this part of the fiber remained apparently normal, but occasionally one could be seen which stained a faint blue. Small lines and buds of different shape were often seen at the outer surface of the layer, some of which, under binocular examination, proved to be ruptured pieces of the layer itself. It may be concluded that basophilia of that part of the elastic fibers of Bruch's layer which dips into the choroid does occur, but is exceptional and slight.

The intense staining of the layer with hematoxylin suggested the possibility of the presence of calcification. The membrane was tested for the presence of calcium, iron, lipoids and amyloid.

The membrane stained by the Kossa method apparently stained faintly (calcium test), more deeply at the posterior pole. It did not, however, stain so intensely as with hematoxylin, and when one remembers that an unstained membrane under an ordinary microscope, but especially a microscope with a narrow diaphragm, can give the appearance of being stained, no definite conclusion is possible. Perhaps the use of ordinary (acid) solution of formaldehyde caused a disappearance of the calcium. The more this possibility was considered the more it seemed probable, since metaplastic bone formed in the eye did not give rise to difficulties in making the sections, though they were not decalcified. Moreover, this

bone did not give a positive reaction to the Kossa test. Control tests with identical results were performed in the pathologic laboratory.[34]

With the iron test for blood pigments it was accidentally found that Bruch's membrane stained intensely, so that there was a pathologic amount of iron in this layer, whereas the rest of the eye was free from blood pigment (fig. 45 *A*). Utmost care and comparative staining excluded the possibility of the iron being due to artefact. In stained

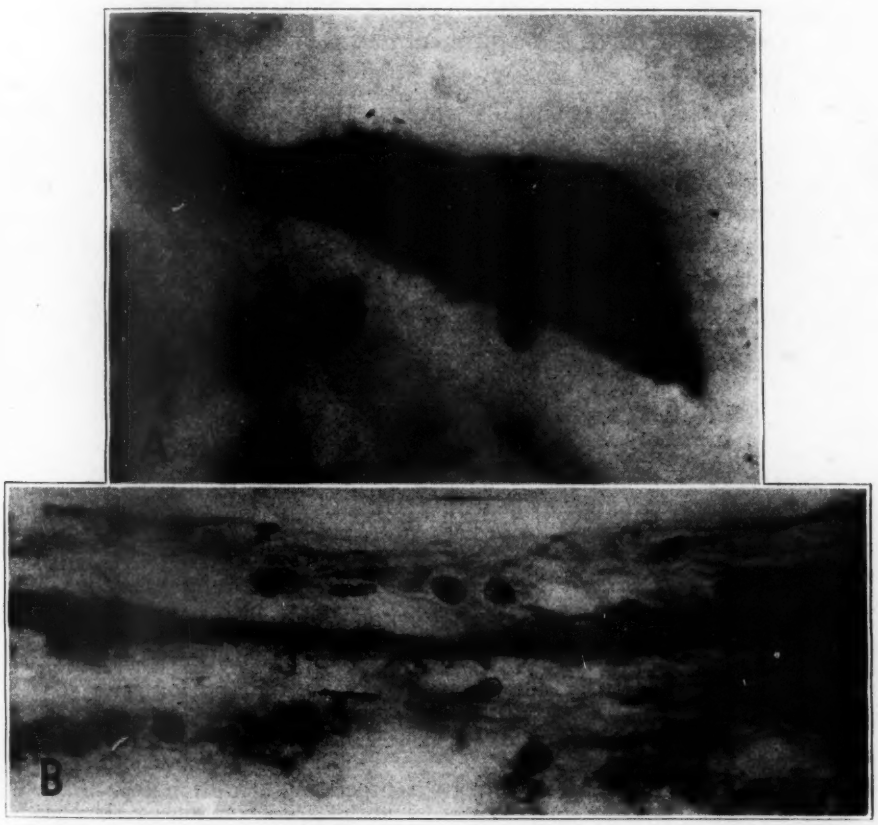

Fig. 19.—*A*, angioid streaks. Damaged pyroxylin section. Hematoxylin and eosin stain; × 1,050. Bruch's layer is twisted and broken and stained with hematoxylin. The fibrillar character is traceable but indistinct. *B*, angioid streaks; macular region. Depigmented specimen. Orcein stain; × 1,050. The last rests of the disappearing Bruch's layer still stain with orcein.

sections of various eyes Bruch's layer was found to give a negative reaction to the iron test. These control sections had been pre-

34. Böck reported the presence of lime but did not perform the Kossa test (Gefässähnliche Netzhautstreifen [Angioid Streaks] und Pseudoxanthoma elasticum, Ztschr. f. Augenh. **86**:238, 1935).

viously handled and preserved in the same way. The possibility exists that Bruch's layer contained calcium in vivo, in connection with which iron was precipitated, since iron has a tendency to precipitate in, or in the neighborhood of, calcified regions. Hueck (according to Schupisser [35]) was the first to demonstrate the affinity of lime for the iron in preserving and staining fluids. But no calcium was present in the sections used for the present study at the time of staining. The results of the test for the presence of iron in the neighborhood of the metaplastic bone were completely negative. This makes it probable that the presence of this iron is independent of a primary presence of calcium.

There may be another source for the presence of iron in Bruch's membrane. It is known that in angioid streaks recurrent smaller and larger hemorrhages may occur. Therefore, the iron in Bruch's membrane might be considered as having originated from former hemorrhages, the blood pigment having completely disappeared from the choroid and retina, whereas it was preserved in the membrane. This, however, cannot be the case, since just the reverse situation was found in siderotic eyes, stained for comparison. It was shown that the pigmented epithelium has an affinity for iron but that Bruch's membrane has not. It remained unstained in eyes with siderosis and hemorrhage, with abundant iron pigment. This finding is not in accordance with Ehrlich's statement (according to and confirmed by Schupisser) that elastic fibers in the neighborhood of hemorrhages have a tendency to become loaded with iron salts. The behavior of pseudoxanthomatous skin to the iron test seemed interesting. I succeeded in obtaining only a piece of pseudoxanthomatous skin, which had been preserved in a solution of formaldehyde for three years. All of the degenerated elastic fibers gave a negative reaction to the Kossa test (calcium); a certain area in the degenerated elastic tissue stained with hematoxylin and was likewise positive to the iron test. It would seem likely, therefore, that siderosis precedes the calcification of the elastic fibers. It is not probable that the iron may have originated from a preceding hemorrhage. I could not find a statement as to whether elastic fibers loaded with iron salts stain with hematoxylin elsewhere. The membrane stained with the Kulschitzky stain, a myelin sheath stain, so that probably lipoids not soluble in alcohol were present, though it must be admitted that this test is not absolutely reliable. Nevertheless, this fact is interesting, since from reports in the literature the appearance of iron, when independent and not secondary to calcium, is always associated with the presence of myelin-like substances (Schupisser). This again supports

35. Schupisser, H.: Ueber Eiseninkrustation der Bindegewebssubstanzen, Virchows Arch. f. path. Anat. **289**:320, 1922.

the view that the presence of iron is secondary not to dissolved but to originally present lime in the elastic fibers. It is regrettable that the foregoing statements cannot be made with certainty, since any calcium present may have been dissolved. They emphasize, however, the importance of handling the material in such a way that any solution of calcium or contamination with iron is prevented. It seems probable, though with some restrictions, that iron plays a role in the process of angioid streaks, although hemochromatosis has not been reported.[36]

There was no amyloid in the membrane or in the other parts of the eye.

Specificity of Involvement of Bruch's Layer.—In studying the collections of specimens showing involvement of Bruch's membrane in the laboratory at the University of Amsterdam, I found a similar basophilia (eye P. A. 980, fig. 20). The eye was enucleated from an old man aged 82 because of pain following an unsuccessful operation for cataract. The posterior segment of the eye was free from inflammation. Bruch's layer stained as it does in angioid streaks, though not so dark. It was impossible to make a photograph similar to that shown in figure 11 *A* on account of the intense pigmentation around the disk. Small patches of the membrane at some distance from the disk had degenerated, but at the equator the membrane was normal. The islands of degeneration resembled those found at the periphery in angioid streaks. It is probable, however, that there is a difference between the degeneration of angioid streaks and that of senility, since in this eye degeneration in the moderately affected areas was more dustlike and individual fibers could not be traced in the sections stained with hematoxylin. Figure 20 shows this degeneration in an area in which pigmentation was less intense. The iron test was slightly positive in the affected areas, the membrane staining a faint blue. This eye further demonstrated the fact that a considerable degeneration of Bruch's layer does not necessarily cause a disciform degeneration of the macula. Ruptures of the membrane were not found.

In eye P. A. 1293 the layer of Bruch stained faintly and homogeneously with hematoxylin. The course of the fibers between the chorio-

36. The iron test was negative in Böck's case; however, the eyes were fixed in Zenker's and Orth's fluid. According to Schmorl, these fluids cannot be used if iron tests should be performed. The Turnbull blue test (after Firmann and Schmelzer) was performed with the specimen studied by me, whereas Böck used the *Berlinerblau* reaction, which is less reliable (*weniger genau* [Romeis], *am wenigsten zuverlässig* [Schmorl]). (See Romeis, B.: Taschenbuch der mikroskopischen Technik, ed. 13, Berlin, R. Oldenbourg, 1932, p. 341. Schmorl, G.: Die pathologisch-histologischen Untersuchungsmethoden, ed. 14, Leipzig, F. C. W. Vogel, 1925.)

capillary layers was easily traceable, since they stained slightly. The specimen was removed from a patient with vascular disease associated with a pale cupped disk and a glaucoma-like field.

The condition which most resembles the degeneration of Bruch's membrane in angioid streaks is senile degeneration of the membrane. Though the differences are notable, still the same has been said by other authors of pseudoxanthoma in relation to senile degeneration of the skin.

The degeneration of the membrane which occurs in disciform degeneration is regarded as the basis of this disease by Behr and Rintelen,

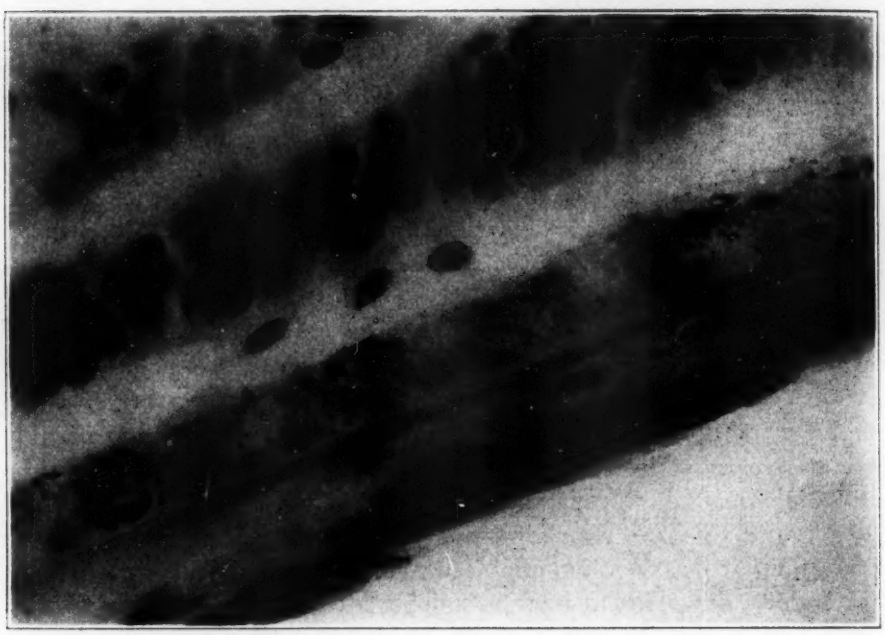

Fig. 20.—Senile degeneration of Bruch's layer. Hematoxylin and eosin stain; × 800. There is dustlike degeneration in the less affected areas.

whereas, on the other hand, Verhoeff expressed astonishment at finding the membrane relatively so well preserved. Doubling of the membrane, as is described in disciform degeneration, was in my sections an optical illusion caused by twisting of the membrane. The affinity of the membrane for orcein was often lost in the reported cases of disciform degeneration, whereas in angioid streaks it is constant. The peripheral parts of the membrane were normal.

Ruptures were present, but small and few in number. Verhoeff expressed the belief that the ruptures are secondary to the activity of the mesodermic cells and stated that "proliferation of connective tissue cells without causing breaks could be definitely recognized." In one of his cases the membrane was broken at but one point, the site of a

Fig. 21.—Choroidal arteriosclerosis. Orcein stain; × 325. There are ruptures of Bruch's layer showing torn fibrillar borders, arteriosclerotic arteries and degeneration of the elastic tissue of the choroid.

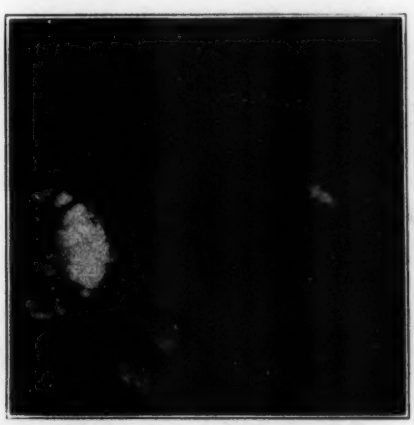

Fig. 22.—Myopia and ruptures of Bruch's layer. The ruptures are closed by cicatricial tissue (white streaks). Note the translucency of Bruch's layer and the visibility of the choroidal vessels.

severe hemorrhage. A good picture of basophilia and rupture in disciform degeneration was given by Wölfflin.[36a] Ruptures of Bruch's layer are likely to occur under various circumstances. Blunt trauma to the eye may cause the membrane to rupture, leaving the retina unimpaired. It is therefore not impossible that it may be found broken in the presence of inflammation. I found a break of the layer in the periphery of a sarcomatous eye, probably traumatic, without reactions of the underlying choroid. Ruptures were found in eye P. A. 1129, which was affected with albuminuric retinitis and choroidal arteriosclerosis (fig. 21); the membrane was not basophilic and looked more torn than broken. High myopia alone produces ruptures which may be compared with those found in angioid streaks. They are seen, however, only in the region of the posterior pole, where their occurrence can be easily explained by the distention of the wall of the eye. Moreover, the membrane is not basophilic, and their form as well as their localization differs from that found in angioid streaks. They are seen, however, only in the region of thickened in angioid streaks. The ruptures are frequently closed by an *Ersatzmembran,* a substitute membrane which gives them the white aspect seen clinically (fig. 22). Nevertheless, it cannot be denied that ruptures occur in myopia which resemble clinically those seen in angioid streaks. On this similarity Kofler [37] founded his theory that angioid streaks are ruptures of Bruch's membrane.

It may be concluded that the described type of degeneration of Bruch's layer is specific for angioid streaks.

(To be concluded)

36a. Wöfflin, E.: Beitrag zur pathologischen Anatomie der Retinitis exsudativa externa, Arch. f. Ophth. **117**:33, 1926.

37. Kofler, A.: Beiträge zur Kenntnis der Angioid Streaks, Arch. f. Augenh. **82**:134, 1917.

CIRCULATORY DISTURBANCES IN RETINA IN ARTERIOSCLEROSIS AND IN ESSENTIAL ARTERIAL HYPERTENSION

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This review is an attempt to correlate the clinical and ophthalmoscopic signs of circulatory disturbances in the retina in arteriosclerosis and in essential arterial hypertension with certain fundamental pathologic elements which underly local circulatory disturbances. These elements are the ones usually discussed in treatises on general pathology under the heading of local circulatory disturbances. I have selected such material from these treatises as is needed for my purpose. Complete discussions are found in standard works, such as those by Aschoff,[1] Hueck,[2] Ricker [3] and Dietrich.[4]

LOCAL CIRCULATORY DISTURBANCES IN AN ORGAN

The circulation of an organ forms a part of the general circulation and is dependent on the general arterial pressure and on the general venous return flow. It also constitutes an independent unit in the service of the particular organ, independent in a way of the general arterial pressure and the general venous return flow and dependent on the needs and activities of the organ at a given time. The arteries, capillaries and veins which constitute the circulatory units are under the control of the vasomotor system, which regulates the degree of constriction and dilatation of the vessels. The local circulatory apparatus can therefore be subject to two kinds of disturbances: (1) vasomotor disturbances, which result from a change in the neural control, and with neural control I shall tacitly include hormonal control, and (2) mechanical disturbances, such as those produced by mechanical obstruction of the lumen of the vessel either by a thrombus or by an embolus within the lumen, by changes in the wall of the vessel or by compression from without.

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1. Aschoff, L.: Pathologische Anatomie, ed. 7, Jena, Gustav Fischer, 1928, vol. 1, p. 461.

2. Hueck, W.: Morphologische Pathologie, Leipzig, Georg Thieme, 1937.

3. Ricker, G.: Pathologie als Naturwissenschaft, Berlin, Julius Springer, 1924.

4. Dietrich, A.: Allgemeine Pathologie und pathologische Anatomie, Leipzig, S. Hirzel, 1933, vol. 1, p. 109.

VASOMOTOR DISTURBANCES

The effect of stimuli on the vasomotor nerves has been shown by Ricker [3] to be as follows: Weak stimuli affect the dilator fibers, causing dilatation of the vessels with an increase in the blood flow. The constrictor fibers are not affected and remain irritable. Slightly stronger stimuli affect the constrictor fibers, causing constriction of the arteries with a slowing of the circulation in the capillaries and veins. Strong stimuli cause paralysis of the constrictor fibers and stimulation of the dilator fibers. This produces at first a dilatation of the vessels and an increase in the blood flow. But the dilator fibers are soon paralyzed, and above the dilated vessel the artery is constricted. The result is a slowing of the blood flow to complete cessation or stasis.

Depending on the action of agents on the vasomotor nerves, there can be distinguished: (1) simple, or active, hyperemia, with an increase in the blood flow (congestive hyperemia), (2) hyperemia, with a slowing of the blood flow, or (3) stasis or cessation of the blood flow.

Simple, or Active, Hyperemia.—Simple, or active, hyperemia is produced by stimulation of the dilator fibers, the constrictor fibers remaining unaffected. Arteries, capillaries and veins are dilated, and the blood flow is increased; there is also an enormous increase in the number of open capillaries. This form of hyperemia is found in a functionally active organ, such as a contracting muscle or a secreting gland. The hyperemia is temporary during activity, and there is only a slight loss of fluid through the capillary wall. Related to this form of hyperemia is the compensatory hyperemia which occurs in the remaining one of a paired organ after the loss of the other; also the collateral hyperemia which occurs in the neighborhood of an infarcted area.

Hyperemia with Slowing of the Blood Flow; Peristatic and Prestatic Hyperemia.—Peristatic and prestatic hyperemia occur with a stimulation of the dilator fibers and a change in the constrictor fibers, which are either diminished in activity or are completely inactive. In the area of the inactive constrictor fibers the arteries, capillaries and veins are dilated, and the circulation is slow and irregular; central to this area the artery is constricted. This form of hyperemia Ricker calls peristatic hyperemia. This classification includes neuroparalytic hyperemia and inflammatory hyperemia. Characteristic for this form is the increased passage of fluid through the capillary walls and its accumulation in the surrounding tissues.

When the artery central to the affected area is still more constricted, there is a still greater dilatation of the vessels in the affected area and a still greater slowing of the blood stream. Ricker calls this form prestatic hyperemia. Circulation is still present but slowed. This form is characterized by the passage of red blood corpuscles through the capillary

walls. They pass through the capillary wall singly at one point, or hemorrhages occur at a number of points.

The peristatic and prestatic forms of hyperemia are of great importance in that they explain the occurrence of edema and hemorrhages.

Stasis.—When the artery central to the affected area is markedly narrowed or completely occluded, the activity of the vasomotor fibers in the affected area is completely lost, the vessels are relaxed and circulation is at a standstill. The capillaries are filled with a column of red corpuscles packed closely to such a degree that the individual corpuscles cannot be recognized. The blood plasma is already lost, having passed into the veins or through the walls of the capillaries into the tissues. The mass of red corpuscles is not agglutinated or thrombosed but simply packed together. With the cessation of the central arterial constriction, the red corpuscles in the static capillary become separated from one another and circulation is resumed. Diapedesis does not occur during the period of stasis, as all movement of red corpuscles has ceased. With long-continued stasis, the tissues supplied by the vessel undergo necrosis.

MECHANICAL DISTURBANCES

The circulation of an organ can be disturbed mechanically by an obstruction to the flow of blood in the arteries or in the veins. Obstruction results (*a*) from compression of the vessel from without, as by an exudate or a growth, or (*b*) from changes within the vessel, such as arteriosclerosis, endarteritis obliterans, thrombosis and embolism.

Complete obstruction of an artery occurring suddenly is followed by a reflex constriction of the vessel peripherally to the point of obstruction and by ischemia of the area supplied by the artery. Soon there occurs a dilatation of the capillaries and venules distal to the constricted area, and, as in vasomotor constriction, there is produced a state of peristasis. From the plasma which is still present in the dilated vessels distal to the constriction or has accumulated there by the backflow from the veins, fluid transudes into the surrounding tissue. When the obstructed vessel is an end artery, such a complete obstruction is followed by an anemic infarct. When the obstruction is not complete, the varying degrees of reflex constriction below the point of obstruction and of dilatation of arterioles, capillaries and venules distal to the constriction produce the conditions of peristasis and prestasis; with the latter, there occur transudation of fluid and hemorrhages to a varying degree.

Obstruction of a vein is followed by cessation of circulation in the vein and by a reflex constriction of the supplying artery. Before circulation stops, there is first a slowing of the blood flow, producing a state

of prestasis with its attendant hemorrhages. Soon a condition of stasis is reached. This type of hyperemia is spoken of as stasis hyperemia.

SUMMARY

Local circulatory disturbances in an organ, whether due to vasomotor changes or to mechanical obstruction, result in various degrees of constriction and of dilatation of the terminal units, leading to states of active hyperemia, peristasis, prestasis, ischemia or obstruction anemia and their consequences.

IMMEDIATE RESULTS OF LOCAL CIRCULATORY DISTURBANCES

Simple, or active, hyperemia is a transitory condition and without any appreciable consequences. Peristasis is accompanied by the passage of fluid through the capillary walls and passes quickly into prestasis, in which hemorrhages occur. Stasis is accompanied by hemorrhage in the prestatic marginal areas, and obstruction anemia is followed by infarction of the involved area. The immediate results of local circulatory disturbances are, therefore, (1) transudation of plasma into the tissues, (2) hemorrhage and (3) infarction.

Transudation of Fluid.—Under normal conditions the passage of fluid through the capillary wall is regulated by the vegetative nervous system in accordance with the needs of the tissues. Hueck [2] has demonstrated that the protoplasm of the endothelial cells of the capillaries and of the basement membrane is capable of undergoing a transitory liquefaction to a degree which permits numerous openings to form which allow the plasma to pass through and, in case of larger openings, also the red corpuscles. In states of peristasis and prestasis the slowing of the circulation in the capillaries causes a diminution in the supply of oxygen and nutrition to the walls of the capillaries and creates the conditions which permit the liquefaction of the protoplasm of the endothelial cells and of the basement membrane. The fluid which transudes is blood plasma and contains a considerable amount of protein; fibrin is then deposited in the tissues.

Hemorrhage.—Hemorrhage as a result of local circulatory disturbances always occurs by diapedesis and practically always occurs through the capillary walls. According to Hueck, such a passage presupposes, as in the case of the passage of fluid, a liquefaction of the protoplasm to a degree which permits openings to form at numerous points. These openings last only for a few moments. They may be close together and in their aggregate permit the formation of large hemorrhages. The immediate cause of such hemorrhages by diapedesis is always a condition of prestasis.

Infarction.—With complete obstruction of an end artery, the tissues supplied by it do not receive any oxygen or nutrition. Death of the tissues occurs at a varying time, depending on the character of the tissue. In the brain it occurs within a few minutes after the obstruction. In the retina it is said to occur after an obstruction of about thirty minutes; in the kidney, after an obstruction of about one hour; in the muscles, after an obstruction of about three hours, and in the skin, after a still longer time. Death of tissue begins in the form of a coagulation necrosis or of a liquefaction. At the margin of the infarcted area there is a condition of peristasis, with dilated vessels, transudation of fluid and hemorrhages.

FURTHER RESULTS OF CIRCULATORY DISTURBANCES

With the removal of the interference of the local circulation, the fluid in the tissues returns to the blood stream, and small hemorrhages are gradually absorbed. When the circulatory disturbance persists, the tissues remain in a chronic state of subnutrition and of deficient oxygen supply, and secondary changes occur. Changes occur also in the extravasated blood, in the infarcted area and in the vascular supply as a consequence of a permanent obstruction of the vessel. These changes are as follows:

1. Changes resulting from a chronically deficient oxygen supply
   (*a*) Visible and stainable fat and lipoid in the tissues
   (*b*) Hyaline deposits

The appearance of such changes where they are ordinarily not visible is always an expression of a chronically deficient oxygen supply.

2. Changes in the extravasated blood
   (*a*) Decomposition of the red corpuscles, with the formation of hematoidin and hemosiderin and their removal by phagocytes, which are also active in engulfing and removing fat, lipoids and hyalin
   (*b*) Organization of a large hemorrhage by the growth of fibroblasts and vessels into it until finally a scar is formed
   (*c*) Formation of a connective tissue capsule around a hemorrhage too large to be completely organized, the blood within the capsule gradually liquefying until a cyst is formed

3. Changes in the infarcted area

The infarct undergoes organization and is gradually converted into a scar. In some organs, such as the brain, the infarct undergoes liquefaction and an area of softening results.

4. Permanent obstruction of a vessel, with the development of a collateral circulation to circumvent the obstruction
   (*a*) By dilatation of anastomotic vessels already present
   (*b*) By dilatation and growth of capillaries and small vessels until they are of sufficient size to maintain the circulation
   (*c*) By formation of new connecting vessels

As an effect of local circulatory disturbances, whether vasomotor or mechanical or a combination of both, the following changes occur in summary:

1. States of peristasis, prestasis and stasis with transudation of fluid and with hemorrhage
2. Infarction, with the conversion of the infarct into scar tissue or into an area of softening
3. The organization or encapsulation of hemorrhage when this cannot be absorbed
4. The formation of a collateral circulation
5. The deposit of fat, lipoid and hyaline material when the oxygen supply to the tissues is persistently inadequate

CIRCULATORY DISTURBANCES IN THE RETINA

The retina constitutes an organ within an organ, namely, the eye. Its circulation is considerably independent of the general circulation and is regulated according to the needs of the retina by the vegetative system, independent of how the circulation is maintained in other parts of the body. Disturbances in the circulation of the retina are caused here as elsewhere by vasomotor changes, by mechanical means or by both. There is an advantage in studying circulatory disturbances in the retina over studying them in other organs in that changes in the fundus of the eye can be directly seen with a magnification of sixteen times. Although the retina itself is transparent, the vascular tree as well as any deformation of the vessels can be seen in detail; and an opaque substance, such as a transudate, a hemorrhage or a hyaline or lipoid deposit, interferes with the transparency of the retina and is readily visible. In view of the preliminary discussion on circulatory disturbances, if one is investigating such disturbances in the retina the following must be looked for: (1) changes in the walls of the vessels, (2) transudation (edema), (3) hemorrhages, (4) fat and lipoid deposits, (5) hyaline deposits and (6) proliferated glial and connective tissue.

The diseases which produce the vasomotor or mechanical changes responsible for the peristasis, prestasis, stasis, obstruction anemia, infarction and their consequences are manifold and include (1) pathologic changes in the walls of the vessels; (2) functional constriction of the walls of the vessels, either localized or as a part of a generalized arterial constriction, and (3) functional constriction superimposed on anatomic changes in the walls of the vessels or preceding these changes.

A few words are necessary regarding the phagocytic elements which engulf particles of hyalin, lipoid and red blood corpuscles. Their origin is not completely determined. Many phagocytes are undoubtedly histiocytes from the adventitia of the vessels. Some are perhaps glia cells. Other phagocytes have definitely been shown to be derived from the

pigment epithelium layer. The cells of this layer are probably not phagocytic, but in the presence of adventitious substances in the retina they are shed and a proliferation of new cells occurs. The newly formed cells contain less and less pigment; they have ameboid movements and are phagocytic. The still pigmented cells gradually lose their pigment, which then becomes an object of phagocytosis and is carried by the phagocytes to the perivascular spaces.

After this preliminary review on local circulatory disturbances, I shall discuss the two most important pathologic conditions which lead to such disturbances and their consequences, namely, arteriosclerosis and essential hypertension.

ARTERIOSCLEROSIS

It is unfortunate that a number of other terms have been used to describe this disease, such as atheroma, atherosclerosis and arteriolosclerosis, which may lead one to assume that each one stands for a different condition.

Arteriosclerosis, "hardening of the arteries," is one and the same disease, whether the intima presents an ulcer with mush in it, an "atheroma," a localized fibrous thickening or a hyaline thickening of the arterioles. As a definition of arteriosclerosis, I may best use the one given by Aschoff:[5]

> We understand by arteriosclerosis a chronic disturbance of the vessels which manifests itself by deposits of the most varied kinds in the vascular walls and which becomes irreversible on reaching its climax in vessels impaired by changes attending the process of aging with resulting deformation of the lumen and brittleness of the vascular wall.

This definition means that the changes due to aging of the arteries, which also causes a thickening of the vascular wall, must be separated from the changes which constitute arteriosclerosis proper. Aging, or senile fibrosis, according to Aschoff, begins at the end of the "stationary period" in life, which is the early forties. It manifests itself by an increase in connective and elastic tissue of the intima and in a reduplication of the marginal elastic layer. The media also shows an increase in the connective and elastic tissue. This causes a thickening and a hardening of the walls of the vessel. The elasticity of this newly formed tissue is less complete, and there occurs at the same time as the thickening of the wall of the vessel a stretching of the wall in all directions. This results in a dilatation of the lumen and in a tortuosity of the vessel, a characteristic of all senile fibrous vessels.

The arteriosclerotic process proper consists of the atherosis, hyalinosis, lipoidosis and nodular deformation added in irregular distribution

5. Aschoff, L., in Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Company, 1933, p. 8.

to the aging process of the vessel. The arteriosclerotic process differs somewhat in the various vessels. In an elastic artery with a well developed intima the process begins with the appearance of fat and lipoids in the cells of the intima and a fine dustlike lipoid deposit in the ground substance (lipoidosis). At the same time there occurs a gelatinous transformation of the ground substance. This area of fatty infiltration increases in size; the center becomes mushy and liquefied and constitutes an atheroma. Meanwhile there is localized growth of elastic and connective tissue between the endothelium lining the lumen and the fatty focus, which prevents the atheromatous mush from breaking into the lumen. When the atheroma does break through, an atheromatous ulcer is formed. In the atheromatous focus fatty acids are set free and attract calcium, which is deposited there. This process of lipoidosis, atheromatous formation, calcinosis and nodular thickening of the intima produces a deformation of the wall of the vessel and constitutes the arteriosclerotic process.

In the muscular arteries of the extremities the process is somewhat different. There the primary process is likely to be a deposit of calcium (calcinosis) in the ground substance of the connective tissue surrounding the muscle fibers. As the deposit of calcium increases, it forms plates, which arrange themselves circularly.

In the arterioles and prearterioles the arteriosclerotic process begins differently. Here the primary process consists of a deposit of hyalin and a hyalinization of the basal membrane underneath the endothelial layer. The hyalinization probably begins as a fibrinoid precipitate, which spreads to the adventitia, melting together ground substance, fibrils and cells. Fats and lipoids are deposited in this hyaline material. Because this process of hyalinosis and lipoidosis is characteristic of the smallest arteries and arterioles, it is spoken of as arteriosclerosis. Fundamentally, it signifies changes following a disturbance in nutrition of the arteriole, just as the primary deposit of fat in the elastic vessel and the primary deposit of calcium in the muscular vessel are the results of a local disturbance in nutrition. The arteriolosclerotic process occurs characteristically in certain organs, especially the spleen, kidneys, pancreas and brain, and is not found in the skeletal muscles.

ARTERIOSCLEROSIS OF THE CENTRAL ARTERY OF THE RETINA AND ITS BRANCHES

NORMAL HISTOLOGIC STRUCTURE

The central artery of the retina, according to Hertel, has a lumen of about 210 microns, narrowing to 170 microns at the lamina cribrosa. In infancy the internal elastic layer lies close to the endothelium. As the arterial branches become narrower, this layer becomes thinner and

can be followed as a layer of longitudinal fibers to arteries of a diameter of 10 microns. According to Friedenwald,[6] the internal elastic lamella disappears entirely beyond the primary branches of the central artery. The media consists mainly of circularly arranged fibers, with here and there some which are arranged obliquely. It also contains some elastic fibers. The adventitia is sharply demarcated from the media and contains elastic fibers in addition to the connective tissue; it merges indistinguishably into the connective tissue surrounding the vessel. As the branches get smaller, the muscle fibers are reduced in number until they can hardly be demonstrated in histologic preparations.

RETINAL ARTERIOSCLEROSIS

Histologic studies of arteriosclerosis of the central artery have been made by Raehlmann,[7] Hertel,[8] Harms,[9] Baumgärtner[10] and Bridgett[11] and others. Baumgärtner's contribution is especially valuable. He found that the development of the artery throughout life corresponds to that of other arteries of the same size. There is a normal physiologic thickening of the intima in the ascending period of life consisting of elastic fibers and interstitial tissue, probably containing muscle fibers. This remains without much change during the stationary period of life, that is, until about the end of the fourth decade. The aging process begins in the central artery, as in other arteries, after 45. This process consists here also in a reduplication in the internal elastic lamella into two or three layers and in an increase of connective tissue. Such a senile thickening in the absence of the arteriosclerotic process was found by Hertel, but Baumgärtner considered its occurrence without regressive changes, such as fatty degeneration, rather rare. Bridgett in a study of the central artery of the retina at 200 autopsies found that during the third and fourth decades it was usually but not always possible

6. Friedenwald, J. V., in Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Company, 1933, p. 363.

7. Raehlmann, E.: Ueber ophthalmoskopisch sichtbare Erkrankung der Netzhautgefässe bei allgemeiner Arteriosklerose, mit besonderer Berücksichtigung der Sklerose der Hirngefässe, Ztschr. f. klin. Med. **16**:606, 1889.

8. Hertel, E.: Beitrag zur Kenntnis der Angiosklerose der Centralgefässe des Auges, Arch. f. Ophth. **52**:191, 1901.

9. Harms, C.: Anatomische Untersuchungen über Gefässerkrankungen im Gebiete der Arteria und Vena centralis retinae und ihre Folgen für die Circulation mit besonderer Berücksichtigung des sogenannten hämorrhagischen Infarktes der Netzhaut, Arch. f. Ophth. **61**:1, 1905.

10. Baumgärtner, H.: Ueber die regressiven Veränderungen der Arteria centralis retinae bei Arteriosklerose, Munich, Thesis, Wiesbaden, J. F. Bergmann, 1914.

11. Bridgett, C. R.: Sclerosis of Central Artery of Retina, Am. J. Ophth. **9**: 725, 1926.

to find a thin, almost homogeneous subendothelial band as well as separation of the internal elastic lamella into a double, and more rarely, into a triple layer. He also found a slight increase in the elastic tissue in the adventitia. At 43 autopsies he found the development of the subendothelial tissue somewhat excessive.

The aging process seems thus to develop in the central artery of the retina in the same manner as it does in other arteries; the arteriosclerotic process is added to this aging fibrosis. Occasionally the arteriosclerotic process is found to occur in young persons. Baumgärtner had a patient of 23 in whom at autopsy fat deposits were found in the intima and one of 33 in whom there was calcification of the elastic fibers in the intima and the media. The arteriosclerotic process begins here also with the appearance of fat and lipoids in the intima. This is followed by formation of atheromas, rupture of the elastic fibers and reparative nodular proliferation of the subendothelial connective tissue; calcium is deposited in the atheromatous areas. Nodular thickening of the wall of the vessel and deformation of the vessel are the results. Baumgärtner found calcification of the elastic fibers in the media with an increase in connective tissue and occasionally also fat and lipoid deposits. The adventitia is affected only slightly or not at all. Hertel, Harms and Baumgärtner found a predilection for the arteriosclerotic process in the region of the lamina cribrosa and in the region of the entrance of the ophthalmic artery into the optic nerve.

The changes in the ophthalmoscopically visible branches of the central artery are similar to those of the main artery but are less common. Friedenwald [12] pointed out "that the ophthalmoscopically visible lesions are merely fringes of a lesion the major portion of which is obscured from view." In the smallest arteries and arterioles, which have no elastic fibers and are not visible ophthalmoscopically, the aforementioned arteriosclerotic process is not found. Here there are found hyalinization and lipoid deposits such as occur in the arterioles and prearterioles of organs like the spleen, kidneys, pancreas and brain. This "arteriolosclerosis" of the retinal arteries occurs in combination with arteriosclerosis of the central artery and its branches under certain conditions, which will be discussed later. It is not, however, part of the picture of arteriosclerosis of the central artery and its branches. In the spleen such an arteriosclerosis is quite common after the age of 10 years and is probably due to local arterial constrictions. It occurs to a marked degree in the kidneys in cases of essential hypertension with renal insufficiency or malignant renal sclerosis. In the retina the hyaline and lipoid deposits in the arterioles and prearterioles occur in association with arterioconstrictive or arteriospastic retinitis.

12. Friedenwald,[6] p. 370.

OPHTHALMOSCOPIC APPEARANCE OF RETINAL ARTERIOSCLEROSIS

In examining the retinal vessels one must keep in mind that the aging process is the same as in other vessels of similar size. It manifests itself in dilatation and tortuosity of the vessels; to these changes is added the irregularly distributed arteriosclerotic process. One must also keep in mind that when looking at a normal vessel with the ophthalmoscope only the blood column is seen and not the wall of the vessel. When there are irregular and patchy changes in the wall they produce an irregularity in the appearance of the blood column. There are, therefore, as a result of the aging plus the arteriosclerotic process, the following signs:

1. A tortuosity of the wall of the vessel. This tortuosity differs from that seen in hypermetropic eyes of young persons and from the congenital variety in that it is more or less angular and does not have the sinuous quality found in the other conditions. In cases of advanced retinal arteriosclerosis it causes the small vessels in the macula to have a corkscrew appearance.

2. Localized variations in the caliber of the vessels. This change is the direct visible expression of localized arteriosclerotic patches. There are all kinds of constrictions in caliber, single or multiple, extending over variable distances, with normal appearing stretches in between the constrictions or with dilatation between them.

3. Localized arteriovenous constriction. This sign was first observed by Gunn.[13] It is seen as an indentation or compression of the vein where it is crossed by an artery. There has been a good deal of discussion as to how the apparent venous constriction is produced and what it signifies. It has been assumed by some authors to be a sign of increase in the general arterial pressure. There is no evidence for this assumption. The most recent contribution is that by Sallmann.[14] He studied the histologic structure of the arteriovenous crossing in a number of persons of all ages with and without hypertension. He found that the artery and vein lie close together where they cross and frequently have a common adventitial coat at this point, an observation previously made by Koyanagi and by Friedenwald. Sallmann found that the vein dips down deep into the retina where it is crossed by an artery, in young persons more so than in older ones. In old persons with or without hypertension there is a thickening of the wall of the vessel and of the common adventitial coat. As the vein dips down, it is hidden by the thickened

13. Gunn, R. M.: Ophthalmoscopic Evidence of (1) Arterial Changes Associated with Chronic Renal Disease, and (2) Increased Arterial Tension, Tr. Ophth. Soc. U. Kingdom **12**:124, 1891-1892.

14. Sallmann, L.: Zur Anatomie der Gefässkreuzungen am Augenhintergrund, Arch. f. Ophth. **137**:619, 1937.

or sclerosed nontransparent wall. Gunn's sign is thus a sign of thickened or sclerosed vessels.

4. Widening of the arterial light reflex. H. Friedenwald [15] pointed out that the width of the light reflex is closely related to the width of the blood column. It would, therefore, be wider in the dilated arteriosclerotic vessel.

These signs, angular tortuosity of the vessels, variations in caliber, apparent arteriovenous constriction and widening of the arterial light reflex, constitute the visible evidence of arteriosclerosis of the retinal vessels. They are found in all degrees of variation. In evaluating them it must be kept in mind that while arteriosclerosis occasionally occurs in young persons, below 40 years of age, it is commonly seen as an addition to the aging process. As the latter begins to manifest itself toward the end of the fifth decade, and as it as well as the arteriosclerotic process are of slow development, it is obvious that the signs of arteriosclerosis described here will become noticeable only in advanced age, in the sixth decade and beyond. This is the normal occurrence. When these signs are found they give visible expression to the degree of the arteriosclerotic process in the retinal vessels themselves; since the central artery of the retina is a part of the cerebral circulation, the signs are a valuable guide to the approximate degree of arteriosclerosis in the brain, and the degree of arteriosclerosis in the retina gives some indication to the degree of arteriosclerosis in the body generally. This is especially true when these signs occur in comparatively young persons, that is, in the fifties or forties or even in younger persons. The wear and tear which blood vessels can withstand are principally dependent on their inherited characteristics, and the signs of wear and tear usually manifest themselves in the senium. When signs of a considerable degree of arteriosclerosis of the retinal vessels are encountered before the senium and in young persons, two etiologic factors must be considered as responsible: first, an inherited deficiency in the wall of the vessel, causing it to give way sooner to the ordinary wear and tear; and, second, an intensification of the wear and tear, causing the vessels to give way prematurely. The one important factor which increases the intensity of the wear and tear of the arterial wall is a persistent increase in blood pressure, especially in the chronic form known as essential arterial hypertension. The finding of signs of arteriosclerosis in the retinal vessels of middle-aged and of young persons calls, therefore, for an immediate investigation as to the presence of a persistent arterial hypertension. Here it is important to make clear distinctions. The signs discussed here, angular tortuosity

15. Friedenwald, H.: The Doyne Memorial Lecture: Pathological Changes in the Retinal Blood-Vessels in Arteriosclerosis and Hypertension, Tr. Ophth. Soc. U. Kingdom **50**:452, 1930.

of vessels, variations in caliber, apparent arteriovenous constriction and widening of the arterial light reflex, are not signs of a general arterial hypertension. They are signs of arteriosclerosis of the retinal vessels. Only their appearance in middle-aged or in young persons serves notice to the observer that something is responsible for their premature occurrence, and the presence of a persistent hypertension may be surmised and must be sought for.

CIRCULATORY DISTURBANCES AS A RESULT OF ARTERIOSCLEROSIS OF THE RETINAL VESSELS

The signs which signify the presence of arteriosclerosis of the retinal vessels do not signify the presence of circulatory disturbances there. Something must be added to produce such disturbances and to create the conditions of peristasis, prestasis, stasis, ischemia and infarction. This something is an interference with the blood flow either in the central artery and its branches or in the central vein and its branches. Such an interference is, as I have previously stated, either mechanical or functional or vasomotor or both. In the central artery and its branches obstruction of the lumen as a result of arteriosclerosis occurs as follows:

1. The local arteriosclerotic lesion extends farther and farther into the lumen until it is completely obstructed.

2. The arteriosclerotic lesion extends into the lumen for a considerable distance, and at its site a thrombus is formed which completely obstructs the lumen.

3. To the arteriosclerotic plaque extending into the lumen there is added a local vasomotor constriction of the vessel, causing complete obstruction.

In the central vein and its branches obstruction of the lumen occurs as a result of phlebosclerosis as follows:

1. The sclerotic process gradually encroaches more and more on the lumen of the vessel, completely obliterating it.

2. To the sclerotic process extending for a variable distance into the lumen there is added a thrombus, which completely occludes the lumen. Obstruction in either the artery or the vein may be complete or incomplete, allowing for some flow of blood. In the artery the obstruction is hardly ever so complete as to cause a total collapse of the vessel; usually a thin plasma stream is still present.

OBSTRUCTION OF THE CENTRAL ARTERY AND ITS BRANCHES

When the clinical picture of obstruction of the central artery was discovered the obstruction was assumed to be due to an embolus, especially as it was frequently found in connection with cardiac disease.

Objections were soon raised to such a view, and the controversy lasted for a long time and is perhaps not over yet. Harms [9] in 1905, in an elaborate study of the reported cases of occlusion of the central artery, came to the conclusion that the presence of a true embolism of the central artery has not been proved anatomically. Still later, in 1925, Scheerer [16] in a critical review came to the conclusion that the anatomic reports of cases of embolism of the central artery in the German literature since 1900 were not able to withstand criticism. He showed that postmortem coagula are frequently found in the central artery of the retina and undoubtedly have been mistaken for emboli or thrombi.

It is necessary to realize that before the early part of this century the differences between bacterial and rheumatic endocarditis were not so well understood. It is now known that emboli do not occur in uncomplicated rheumatic endocarditis. Since occlusion of the central artery occasionally occurs in rheumatic valvular disease, especially in mitral stenosis, such an occlusion cannot be caused by an embolus. More logical is the assumption that such an occlusion in mitral stenosis is caused by a functional constriction of the artery. In cases of acute and subacute bacterial endocarditis in which emboli are continually thrown into the blood stream it is probable that they are occasionally lodged in the central artery or its branches. However, from the literature on bacterial endocarditis it is difficult to determine how often such emboli occur in the central artery in the course of this disease.

CIRCULATORY DISTURBANCES AS A RESULT OF OCCLUSION OF THE CENTRAL ARTERY OR ITS BRANCHES

The clinical picture of occlusion of the central artery is well known. The essential features are: (1) sudden loss of vision; (2) narrowing of the arteries, in which a thin line of slowly moving blood is seen, sometimes having a granular or broken-up appearance; (3) inability to produce arterial pulsation by pressure on the globe, and (4) milky white appearance of the central part of the retina in which the nonedematous fovea appears as a red spot. A small hemorrhage may be found here and there in the retina but is, strictly speaking, not part of the clinical picture.

When the edema has subsided there remains finally (1) a pale atrophic optic disk with sharp distinct edges and (2) very narrow arteries, which are accompanied here and there near the disk by fine white lines for a short distance.

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16. Scheerer, R.: Ueber Vorkommen und Bedeutung freier Blutpfröpfe im Stamme der Zentralgefässe, Arch. f. Ophth. **115**:370, 1925.

The occlusion of a branch of a central artery is characterized by similar symptoms in the area of the retina supplied by that particular branch.

With an understanding of the processes involved in local circulatory disturbances, it is easy to follow the happenings in the retina in occlusion of the central artery, whether it is of mechanical or of functional origin. After the occlusion, there is a reflex constriction of all the arterial branches and, to a lesser degree, of the veins. The arterial constriction immediately creates the conditions for a state of peristasis and prestasis. The terminal units of precapillary arterioles, capillaries and postcapillary venules dilate, and plasma transudes into the surrounding retina. The transuded fluid causes a swelling of the inner layers of the retina. Where the inner layers are missing, in the fovea, the normal color contrasts sharply with the white of the edematous retina. The absence of hemorrhage or its occasional occurrence only is to be explained by the red corpuscles being prevented from entering the terminal units by the obstruction above. When the interruption of the blood supply is maintained for a certain period (said to be not more than half an hour, although this is doubtful), there is an anemic infarction of the inner layers of the retina. The nerve fibers, the ganglion cells and the inner nuclear layer die, and phagocytes make their appearance. Within a period of time, weeks or months, the edema recedes, hyaline and fat deposits appear here and there, any hemorrhage is absorbed and there is an increase in glial and connective tissue which gives the retina a shagreened appearance. Glial and connective tissue also appear as white lines along some of the vessels for variable distances. The end result is a retina with a thin atrophic inner layer in which there are few nerve fibers, few nerve cells and only the single layer of nuclei belonging to Müller's fibers.

The occlusion of any branch of the central artery has a similar train of processes in its wake: constriction of the artery peripheral to the obstruction, dilatation of the terminal units, transudation of plasma and perhaps a few hemorrhages; then follows disappearance of the transudate, hyaline and lipoid deposits, appearance of phagocytes, increase in glial and connective tissue and, finally, atrophy of the part of the retina supplied by that particular branch.

Obstruction of the Central Vein.—Obstruction of the central vein occurs most frequently at the lamina cribrosa, and obstruction of a venous branch, at a point where it is crossed by an artery. It is characterized clinically and ophthalmoscopically by (1) diminution of vision to a variable degree, from the counting of fingers to perception of hand movements in some cases; (2) redness of the optic disk and blurring of its margins; (3) narrowing of the arteries; (4) dilatation and tortuosity of the venous branches, which may be two or three times their

normal caliber; (5) absence of arterial pulsation and of collapse of the veins on pressure on the globe; (6) single and confluent hemorrhages of all sizes and shapes (flame shaped, radial and round), extending widely from the optic disk to the periphery and occasionally into the vitreous, and, later, (7) white or yellowish white deposits of hyalin and lipoids within the areas of hemorrhage.

Obstruction of a branch of a central vein produces a similar train of symptoms localized to the area of the retina which the venous branch drains.

When the obstruction is incomplete, all the signs are less marked.

The circulatory disturbances can be traced here. When the hindrance in the central vein is sufficiently large to obstruct the flow of blood, there is a slowing of the blood stream and a dilatation of the veins above the obstruction. This slowing extends backward to the small venules, capillaries and arterioles. With the slowing of the circulation, the stage of peristasis passes quickly into one of prestasis and then into one of stasis. At the same time there is a reflex constriction of the branches of the central artery. The numerous hemorrhages occur during the prestatic state. When the blood begins to be absorbed, the deficient oxygen supply is responsible for the appearance of hyaline and lipoid deposits. Some of the white spots are found to consist of ganglioform enlargement of nerve fibers. With an incomplete obstruction of the central vein, the same sequence of events occurs.

The further consequences of obstruction of the central vein are: (1) the development of a collateral circulation and (2) atrophy of the inner layers of the retina and hypertrophy of the supporting glial and connective tissue.

The development of a collateral circulation occurs in the manner previously described. The new anastomotic vessels have various forms, straight or curved, connecting the obstructed branch with a neighboring vein, or they form tortuous glomerular networks of all shapes and sizes. Frequently they are found in proliferated connective tissue which projects into the vitreous.

Of great clinical importance is a complication of occlusion of the central vein, namely, secondary glaucoma; but this is not a subject for discussion here.

Obstruction of Very Small Arteries and Veins.—It is necessary to discuss separately the obstruction of small arteries and veins. Such a small vessel may become obstructed either by a local proliferative change in its walls or by functional constriction. When such a small artery is obstructed, there is a localized area of edema, seen as a fluffy white spot; the obstructed vessel may not be visible. It is not an uncommon occurrence and causes a small relative or absolute scotoma. When a small vein is obstructed, one or more hemorrhages are the result. In the

periphery of the retina the blood supply is scanty, and with the aging process the number of capillaries there is gradually reduced. This leads to a thinning of the already thin retina at this point and to the formation of cystoid spaces. Vogt[17] has pictured obliterated vessels leading to peripheral areas of cystoid degeneration.

There is one area in the retina in which retinal capillaries do not exist, namely, the fovea. Obliteration or occlusion of small arterioles leading toward the macula will result in peristatic edema and later in atrophy and cystoid degeneration of the retina at this point and finally in the formation of a hole. This process can be followed occasionally from its inception to the formation of a hole.

A similar process occurs with the occlusion of a small vein in the macula, leading to prestasis with hemorrhages and then to stasis. In the macular area such a hemorrhage after absorption is followed by atrophy of the retina, cystoid degeneration and the formation of a hole. I have been able to follow 2 such cases from the obstruction of a small vein in the macular region to the formation of a hole there.

ESSENTIAL ARTERIAL HYPERTENSION

In discussing arteriosclerosis, I have said that normally the arteriosclerotic process which adds itself to the aging process becomes manifest in old age, in the sixties and seventies, but rarely in the fifties. When arteriosclerosis becomes visible in persons of middle age or in younger persons, one of two factors or both can be held responsible for its early appearance: (1) an inherited deficiency in the walls of the vessels, which causes them to undergo earlier the changes due to wear and tear; and (2) an undue intensification of the wear and tear of the walls of the vessels. As a cause of such an intensification, I mentioned persistent arterial hypertension.

Persistent arterial hypertension occurs in two forms: as an accompaniment of diffuse glomerulonephritis and of malignant renal sclerosis and as essential arterial hypertension. There are distinct differences between the two forms, even as to the appearance of the patient. Persons with diffuse nephritis look pale. Volhard called them "pale hypertensives," in contrast to the full-blooded appearance of persons with essential hypertension, whom he characterized as "red hypertensives." There is also a fundamental difference between the two forms which affects their pathogenesis, course and outcome. This difference consists in the presence of a generalized arterial constriction of the small arteries in diffuse glomerulonephritis and malignant renal

17. Vogt, A.: Ueber zystoide Retinaldegeneration und die begleitenden Linien-netze, und über die optischen Bedingungen der Sichtbarkeit der Zystem, Klin. Monatsbl. f. Augenh. **92**:743, 1934.

sclerosis and in the absence of such a constriction in essential arterial hypertension. I shall discuss essential hypertension and review briefly my conception of this disease.

THE MAINTENANCE OF NORMAL BLOOD PRESSURE

The normal blood pressure of an adult ranges from 110 to 140 mm. of mercury systolic and from 60 to 90 mm. diastolic. An increase above 150 mm. systolic and above 100 mm. diastolic is abnormal. The maintenance of the normal arterial pressure is one of the physiologic norms which has been evolved phylogenetically as an optimum for the organism and which the organism maintains at a constant value within normal limits of variation by means of a regulatory mechanism. This mechanism consists of: (1) effector organs, which are the muscle fibers in the arterial walls in which the contractile tonus is maintained by a balance of certain electrolytes; (2) a vasomotor center in the brain, which regulates the degree of contraction of the muscle fibers; (3) vasomotor fibers, through which the center exerts its regulation, and (4) hormones, especially of the posterior lobe of the hypophysis, another means by which the center in the brain exerts its regulation on the muscle fibers. The whole constitutes a unit mechanism which adapts itself easily to the demands of the body and maintains the arterial pressure at a normal level. This mechanism is ordinarily effective throughout life but is likely to lose its stability in old age when variations in blood pressure become noticeable.

PATHOGENESIS OF ESSENTIAL ARTERIAL HYPERTENSION

In following the course of the blood pressure in a person in whom essential hypertension eventually develops the following sequence of events is observed: In middle life, that is, in the forties or earlier, and in an occasional young person, there are noticed a greater lability and a loss of stability of the normal arterial pressure. There are periods of variation in which the blood pressure rises to 160 mm. and higher, only to return to normal at other periods. The rise in pressure may occur during part of a single day or may last for many days. Essentially these variations are an exaggeration of those occurring in normal persons of that age. With the passing of an indefinite period of time, perhaps a number of years, the variability of the blood pressure still persists, but the pressure returns much less frequently to normal and persists more and more at a higher level, perhaps around 160 or 170 mm. of mercury. With the passing of a further period, the greater variability is still present or is even more marked, but now the blood pressure is permanently high, perhaps around 200

mm. of mercury or higher. The intensification of the wear and tear as a result of the persistently high blood pressure has exercised its influence on the arteries, and both the aging and the arteriosclerotic processes have become intensified, and pathologic changes in the arteries are noticeable. It is evident that the mechanism for the maintenance of the normal arterial pressure is fundamentally defective in such a person and loses its stability at an early age. The cause of the loss of this stability has not been found in any external factor or in any general disease. The only factor known is that of heredity. This factor in essential hypertension has been studied especially by Weitz,[18] and the subject is thoroughly reviewed by Williams.[19]

I conceive essential arterial hypertension to belong to a group of diseases which are characterized primarily by the comparatively early loss of stability of the mechanism for the maintenance of a normal physiologic value. In a previous publication[20] I have included in this group besides essential hypertension also diabetes and chronic simple glaucoma. I define essential arterial hypertension as a disease in which there occurs in some persons in middle life and occasionally earlier a loss of stability in the mechanism for the maintenance of the normal arterial pressure. This loss of stability is the result of an inherited defect already present in the germ plasm. It manifests itself at first by variations in the height of the blood pressure which are exaggerations of the normal variations. Eventually there is a complete loss of ability to maintain the normal blood pressure, which remains now at a high level. With the persistence of the high level of blood pressure, the aging and the arteriosclerotic processes are hastened and appear earlier in life.

THE VASCULAR CHANGES IN ESSENTIAL HYPERTENSION

Since essential hypertension is a disease which begins with a variability in the height of the blood pressure in middle life and extends into old age, it is obvious that any secondary arterial changes will vary with the duration and the degree of the hypertension. In the early years there are practically no changes in the arterial system beyond the ones appropriate for the age period. With the passing of years, the aging and arteriosclerotic processes appear more and more. It is characteristic for this disease that these processes particu-

18. Weitz, W.: Zur Aetiologie der genuinen oder vaskulären Hypertension, Ztschr. f. klin. Med. **96**:151, 1923; Studien an eineiigen Zwillingen, ibid. **101**: 115, 1925.

19. Williams, G. D., in Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Company, 1933, p. 537.

20. Elwyn, H.: Pathogenesis of Chronic Simple Glaucoma: New Concept of Maintenance of Normal Intraocular Pressure, Arch. Ophth. **19**:986 (June) 1938.

larly affect the vessels of the kidney. In some persons these vessels are exclusively affected; in others, they are affected long before other vessels. It is for this reason that essential hypertension is also spoken of as benign renal sclerosis.

The characteristic changes in the vessels of the kidneys are as follows:

1. In the medium-sized and small arteries there is a thickening of the intima consisting of a multiplication of the elastic lamella with an increase of connective tissue between the lamellae. The muscular layer is reduced in thickness. This process is diffuse throughout the vessels. In the hypertrophied intima there occur regressive changes, namely, hyaline and lipoid deposits in an irregular focal distribution.

2. In the arterioles there are deposits of hyalin and lipoid which cause a thickening of the walls of the vessels. These deposits are not diffuse throughout all the vessels but are found in some and not in others, and in those affected they are not present throughout the whole vessel. These deposits increase in extent with the duration of the hypertension.

Other arteries in the body may be free from any disease. However, with the progress of the hypertension the arteriosclerotic process begins to appear here and there in a focal distribution in other arteries. In many instance the arteriosclerosis is widespread, affecting the aorta and its branches, the arteries of the heart and of the brain. The arteriolosclerotic process is found most frequently in the kidneys only; in some cases and in those in the advanced stage it is found also in the pancreas, less frequently in the liver and occasionally in other organs. The arterioles of the extremities are not affected.

CHANGES IN THE VESSELS OF THE RETINA IN ESSENTIAL HYPERTENSION

In the early stages of essential hypertension, and sometimes even in the advanced stages, there are no changes in the vessels of the retina to indicate a premature aging or the presence of arteriosclerosis. In many cases, perhaps in most, the prolonged intensification of the wear and tear affects the vessels of the cerebral circulation and with it the arteries of the retina. There is then noticed ophthalmoscopically the premature appearance of signs of arteriosclerosis in the retinal vessels, angular tortuosity, variations in caliber, widening of the light reflex and apparent venous constriction where a vein is crossed by an artery. A certain degree of fulness or plasticity of the vessels which makes them stand out clearly is noticed in some cases. There is nothing in these signs which is characteristic of essential hyper-

tension. It is their early appearance and their manifestation to an unusual degree which calls attention to the possible presence of arterial hypertension.

COMPLICATIONS

With its earlier development, arteriosclerosis becomes intensified in years. All the complications mentioned in the discussion on arteriosclerosis of the retinal vessels occur here more frequently and earlier: occlusion of the central artery or its branches and occlusion of the central vein or its branches or a combination of both. Circulatory disturbances leading to peristasis, prestasis, stasis and infarction occur with these complications.

Aside from these more marked complications, there occur occasionally in the retinal vessels in cases of advanced essential hypertension two processes which lead to local circulatory disturbances.

1. A marked degree of tortuosity, dilatation of some tiny vessels and constriction of others are found irregularly distributed in the very small vessels. These irregular dilatations and constrictions lead to circulatory disturbances in small areas and states of peristasis, prestasis and stasis. Small hemorrhages, pinpoint and larger; small patches of transudate, which quickly disappear, and small deposits of hyalin and lipoids, which either disappear or remain, appear in the areas of the retina supplied by these small vessels.

2. The second process is of more serious import. I have said that essential hypertension is a disease in which the mechanism for the maintenance of the normal blood pressure has lost its stability and has become more labile. The loss of stability once begun increases in years. With it there occur occasionally episodes in which without any apparent reason there is a sudden increase in blood pressure, which rises to 250 or 300 mm. of mercury, only to return to the previous level after a variable period of time. During such an episode there may occur temporarily a generalized constriction of small arteries or a localized constriction of the arteries of some individual organ, including also those of the brain and of the eyes. The occurrence of such episodes has long been known. They have been described by Osler [21] as "transient attacks of aphasia and paralysis in states of high blood pressure and arteriosclerosis." These attacks are frequently a precursor of a more serious change in the tempo of progress of the disease.

When these attacks occur suddenly with a generalized constriction of the small arteries and a sudden rise of blood pressure, there is likely to occur a sudden increase in intracranial pressure as a result

21. Osler, W.: Transient Attacks of Aphasia and Paralyses in States of High Blood Pressure and Arteriosclerosis, Canad. M. A. J. 1:919, 1911.

of edema of the brain. This reacts on the eyes as does any increase in the intracranial pressure. Ophthalmoscopically, there is seen a swelling of the disk, which varies from a blurring of its margins to a swelling of several diopters. There is the usual accompaniment of hyperemia of the veins, narrowing of the arteries and hemorrhages. With the subsidence of the attack and the return of the blood pressure to the previous level, the swelling of the disk recedes. The hemorrhages are gradually absorbed and the vessels regain the appearance which they had before the attack. Some hyaline and lipoid deposits may be seen.

Such an attack may be the only one, or it may recur; or, instead of receding, the swelling of the optic disk may remain for months after the acute cerebral symptoms have disappeared and the patient is otherwise quite well.

The occurrence of such an attack of generalized arterial constriction in the course of essential hypertension is significant of a change in the progress of the disease, especially when the occurrence is repeated. The disease is about to lose its benign character and will within a variable period of time pass into malignant renal sclerosis.

THE MALIGNANT PHASE OF ESSENTIAL ARTERIAL HYPERTENSION OR MALIGNANT RENAL SCLEROSIS

In discussing essential hypertension, I mentioned the occasional occurrence in some cases of transient arterial constriction generally or locally in the brain and also in the retina. This transient constriction results in local circulatory disturbances. I come now to the cases of essential hypertension in which there occurs after a long period of hypertension a generalized constriction of the small arteries which is not transient but permanent. In these cases the hypertension occurs earlier in life and is more marked, from 200 to 300 mm. of mercury systolic and from 140 to 190 mm. diastolic. Volhard rendered a great service when he discovered that it is the added general arterial constriction which almost suddenly converts the relatively benign essential hypertension or benign renal sclerosis into the malignant renal sclerosis with progressive renal insufficiency.

Pathologically, the arteriosclerotic and arteriolosclerotic processes are markedly advanced in the kidneys. There are found: (1) a diffuse thickening of the intima and a multiplication of its elastic layers in the larger and smaller arteries; (2) a cellular and fibrous proliferation in the intima of many small arteries forming an obliterating endarteritis; (3) marked hyaline and lipoid deposits in the proliferated intima of the small and smallest vessels, including the arterioles; (4) hypertrophy of the muscular layer in the medium-sized and small arteries; (5) a necrosis of the walls in some of the thickened arteri-

oles, with nuclear disintegration and with evidence of hemorrhage in the walls; and (6) correspondingly severe changes in the glomeruli and tubules.

Pathologic changes in the vessels have been found in other organs, in the pancreas, spleen, liver and brain, but they are much less marked than in the kidneys and are frequently slight.

In the retina the pathologic changes in the vessels have been recently studied by de la Fontaine Vervey,[22] Kyrieleis,[23] Friedenwald [6] and Garsteiger.[24] These investigators have found arteriolosclerosis, that is, thickening of the prearterioles and arterioles due to the deposit in the vessels of hyalin, fat and lipoid. Lipoids were also found in the small vessels of the optic nerve. There was also hypertrophy of the muscular coat. In addition to the arteriolosclerosis, there is an intensification of the aging and arteriosclerotic processes in the larger vessels, with nodular thickening of the intima to varying degrees. With these changes in the vessels there are found all the pathologic changes of arterioconstrictive retinitis: edema, hemorrhage, cystoid spaces filled with plasma and fibrin, hyaline, fat and lipoid deposits, phagocytes and ganglioform swelling of nerve fibers.

Ophthalmoscopically there are seen: (1) signs of advanced arteriosclerosis and arteriolosclerosis, consisting of angular tortuosity of the vessels, especially the small ones, variations in the caliber of the lumen, apparent constriction of veins where they are crossed by arteries and a sharp and bright light reflex with irregularity in its width; (2) arterioconstriction, as shown by the narrowed arteries, especially the smaller branches; (3) signs of local circulatory disturbances of acute character, consisting of edema, hemorrhages, cotton wool patches, blurring of the margins of the optic disk and distinct papilledema, and (4) sharp white spots of hyaline deposits, glistening spots and the star figure in the macular area.

Pathologic changes occur also in the vessels of the choroid, and choroidal arteriosclerosis is frequently seen.

Complications of arteriosclerosis, occlusion of the central artery or vein or of their branches, occur in some cases.

The whole clinical picture in the fundus represents the local circulatory disturbances as a result of a persistent and varying arterial

22. de la Fontaine Vervey, B. C.: Ueber die Arteriolosklerose der Netzhaut und ihre Bedeutung für die Genese der Retinitis albuminurica, Klin. Monatsbl. f. Augenh. **79**:148, 1927.

23. Kyrieleis, W.: Ueber die Arteriosklerose von Netzhaut, Aderhaut und Sehnerv sowie ihre Bedeutung für die Pathogenese der Retinitis albuminurica, Arch. f. Augenh. **103**:161, 1930.

24. Garsteiger, H.: Ueber histologische Befunde am Auge bei Nieren- und Blutdruckveränderungen, Klin. Monatsbl. f. Augenh. **99**:604, 1937.

constriction which has suddenly been added as a malignant factor in the course of an essential hypertension. There is no doubt at this stage of knowledge that the general arterial constriction is responsible for the changed character of the disease, for the appearance of renal insufficiency and for the cerebral and the retinal symptoms. Klemperer and Otani,[25] in discussing Volhard's angiospastic theory from the pathologist's point of view, remarked:

> It is conceivable that a constitutional or acquired angiospastic factor could be the reason for the severity and especially for the acceleration of the vascular process which is the outstanding characteristic for the differentiation between vascular diseases of the kidney with and without functional insufficiency.

CONCLUSION

I have reviewed two of the most important diseases of the retinal vessels which are responsible for circulatory disturbances in the retina. These diseases have two components: (1) organic, with changes in the vessels which interfere with the normal blood flow, and (2) functional, leading to constriction of the vessels. Whether the interference with the normal blood flow is due to organic changes or to functional constriction, the result is the production of local circulatory disturbances in the retina which are similar. These disturbances follow the dilatation of the terminal units of the vascular system, precapillary arterioles, capillaries and postcapillary venules, with constriction of the artery above. Depending on the degree of constriction and dilatation, there occurs peristasis with transudation of fluid, prestasis with hemorrhages, stasis with stoppage of the circulation or infarction. With the release of the constriction and the resumption of the normal blood flow, the transuded fluid and the hemorrhages are absorbed. When the interference with the blood flow persists but the blood supply to the retina is not completely restricted, the chronic suboxidation and subnutrition of the retina manifests itself by deposits of hyalin, fat and lipoids. When infarction occurs, collateral circulation with the formation of all forms of anastomotic vessels is established whenever possible. Hemorrhages that are too large to be absorbed stimulate connective tissue formation and are either organized and converted into scars or are encapsulated.

These consequences of the dilatation of the terminal vessel units and the constriction of arteries above appear in the retina in various forms in the diseases discussed. They can be seen and studied in the retina better than anywhere else in the body. An appreciation of the manner of their production helps in the understanding of the diseases so far as they affect the retina.

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25. Klemperer, P., and Otani, S.: "Malignant Nephrosclerosis" (Fahr), Arch. Path. **11**:60 (Jan.) 1931.

PRIMARY GLIOMA OF THE OPTIC NERVE

REPORT OF A CASE

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LOS ANGELES

Largely as a result of Hudson's [1] comprehensive paper, tumors of the optic nerve have been divided into those of the nerve itself and those of the nerve sheaths. At present most pathologists consider the first group to be gliomas of the spongioblastic type and the second to be endotheliomas or meningiomas and the various fibromas, with rare instances of sarcoma and angioma. It is with the first group, the primary intraneural tumors of the optic nerve, that we are at present concerned.

Glioma of the optic nerve is rare. Less than 300 examples of this tumor have been described in all the medical literature.[2] During a period of thirty-six years at the Massachusetts Eye and Ear Infirmary only 4 such tumors were removed from 669,857 new patients. From the Wills Hospital in Philadelphia DeLong [3] reported that during a period of twelve years only 1 such tumor was found in 230,742 patients admitted. The ratio between gliomas of the optic nerve and sarcomas of the choroid has been found to be about 1 : 200.[2] Hudson [1] observed that primary glioma of the optic nerve was more frequent in the female sex and occurred in the first decade of life in about 75 per cent of the cases. In 1 instance, however, the tumor was discovered as late as the sixtieth year.

Investigation of the literature reveals a confusion of terminology and emphasizes the not infrequent involvement of the intracranial portions of the nerves and chiasm by the neoplasm.

Embryologically, the optic nerve arises from an invagination of the primitive cerebral vesicle and therefore contains all the adult forms of neuroglia. For this reason the same variety of neuroglial tumors

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1. Hudson, A. C.: Roy. London Ophth. Hosp. Rep. (pt. 3) **18**:317, 1912.

2. Verhoeff, F. H., in Penfield, W.: Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1932, vol. 3, p. 1029.

3. DeLong, P.: Am. J. Ophth. **17**:797, 1934.

found in the brain might be anticipated in the optic nerve. Up to the present time, however, the polar spongioblastoma is the type invariably described. Although instances of fairly rapid growth during the course of several months are not rare, glioma of the optic nerve, in contradistinction to the retinal glioma grows slowly in the vast majority of cases.

Glioma of the optic nerve presumably advances by direct extension along the intraneural portion of the nerve, does not invade the dura and does not metastasize. Although extension to the chiasm and deeper structures of the brain may occur fairly often, invasion of the disk has been reported in only 4 or 5 instances. The tumor may spread from the intraorbital to the intracranial portion of the optic nerve through the optic foramen, or from the intracranial to the intraorbital portion of the nerve. In the majority of cases reported the neoplasm has occurred in the intraorbital portion. The growths in 20 per cent of Hudson's cases involved both the intraorbital and the intracranial portion.

One of the earliest reported examples of extension into the chiasm was that of Heymann [4] in 1842, a "neuroma nervi optici." The first reported attempt at intraorbital enucleation for sarcoma of the nerve was made by Ritterich [5] in 1861, with fatal results. At autopsy an enormous enlargement of the chiasm was found. Subsequently such growths were treated surgically, among them 3 described by von Graefe,[6] a "sarcoma myxomatodes" and a "myxoma" in 1864 and a glioma in 1866. The last-mentioned growth occurred in a child of 6 who had exophthalmos due to a tumor of the nerve. At operation the globe was removed and the retrobulbar tumor partially extirpated. Meningitis followed, and autopsy revealed what Virchow termed a "gliosarcoma" involving the intracranial portion of both optic nerves, the optic chiasm and the base of the brain.

In 1922 Dandy [7] stressed the fact that a high proportion of intraorbital tumors of the optic nerve may and do extend into the cranial chamber. He emphasized the futility of operations on the orbital part of such tumors, pointing out that a false sense of security may result and more complete surgical intervention by the intracranial approach be delayed until the condition has become hopeless.

Verhoeff [2] observed that Hudson [1] was unable to discover any reported cases of orbital recurrence, even though in many cases the

4. Heymann, A.: De neuromate optici, Berlin, 1842.

5. Ritterich, F. P.: Weitere Beiträge zur Vervollkommnung der Augenheilkunst, Leipzig, C. F. Winter, 1861, p. 57.

6. von Graefe, A.: Arch. f. Ophth. **10**:193, 1865; cited by Martin, P., and Cushing, H.: Arch. Ophth. **52**:209, 1923.

7. Dandy, W. E.: Am. J. Ophth. **5**:169, 1922.

removal had been incomplete. Verhoeff also found, on the basis of clinical and postmortem evidence, that in most cases the tumor originated in the intraorbital portion of the nerve but soon extended through the optic canal to involve the chiasm. The lack of orbital recurrence is then unimportant in the face of possible intracranial extension of the

Fig. 1.—Preoperative photograph of the patient taken on April 13, showing the outward and downward exophthalmos of the right eye.

Fig. 2.—Roentgenograms of the optic foramens, taken on April 11: *A*, dilated right optic foramen, and *B*, normal left optic foramen.

neoplasm, which leads to a fatal termination once the chiasm is involved. It is surprising that the early examples of intracranial extension failed to leave much impression on many subsequent writings concerning these tumors.

REPORT OF CASE

History.—J. P., a boy of 4½ years, was admitted to the Children's Hospital from the outpatient department on April 8, 1938, with a history of slowly progressive unilateral exophthalmos, of the right eye, during the preceding year. Coincidentally, there occurred an outward and downward protrusion of the eye, with no apparent distress to the patient. The child was otherwise well. Nothing of significance was discovered in the family or the past history.

Examination.—On admission to the hospital the child appeared well and active except for exophthalmos of the right eye and was little concerned about the condition of the eye. The globe was displaced downward and outward (fig. 1). There was marked limitation of upward movement and slight limitation of inward movement. No resistance was felt when the eye was pushed back into the orbit. The exophthalmos was nonpulsatile. The right pupil was slightly dilated and reacted sluggishly to light. Vision in this eye was reduced to 2/200. Projection of light was good in all fields. The intraocular tension was normal to palpation.

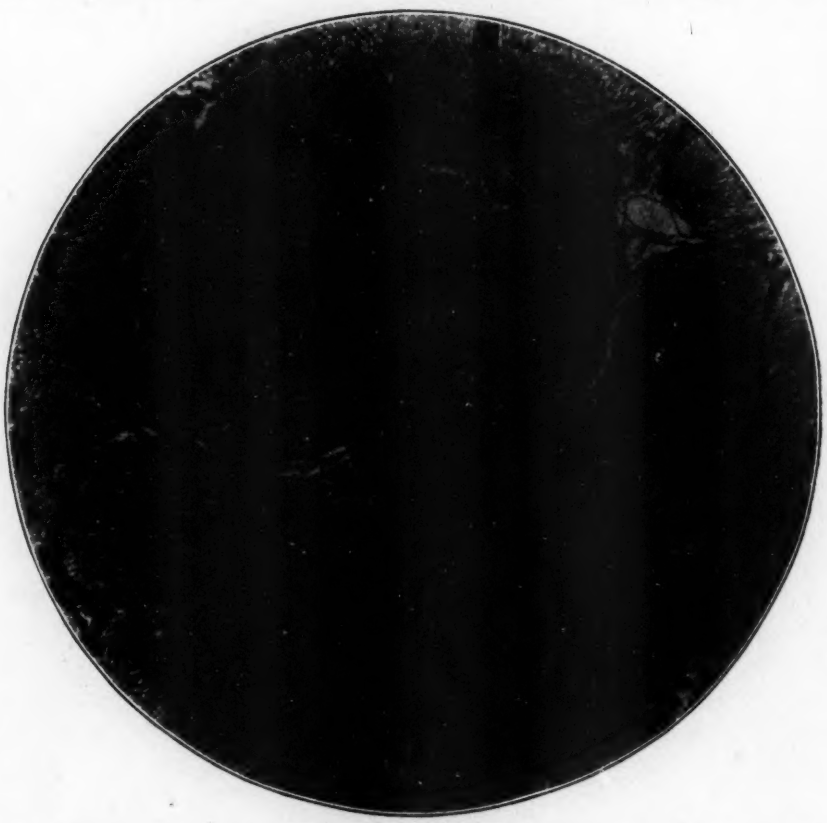

Fig. 3.—Low power photomicrograph of a cross section through the glioma of the optic nerve, showing bands of connective tissue representing the normal fascicular architecture of the nerve with intervals between occupied by typical gliomatous tumor.

The ophthalmoscope revealed clear media and a slightly grayish optic disk, with definitely fuzzy margins. The retina was somewhat pale on the nasal side of the disk, giving the appearance of having been stretched. The macula had a slightly granular appearance. The arteries were normal; the veins were questionably dilated. There was no pulsation in the vessels. There were no hemorrhages or exudates. The left eye was normal, with vision of 20/20. Both corneal reflexes were equal and active. Satisfactory visual fields could not be obtained because of the inability of the patient to cooperate. The results of general neurologic and physical examinations were otherwise entirely negative.

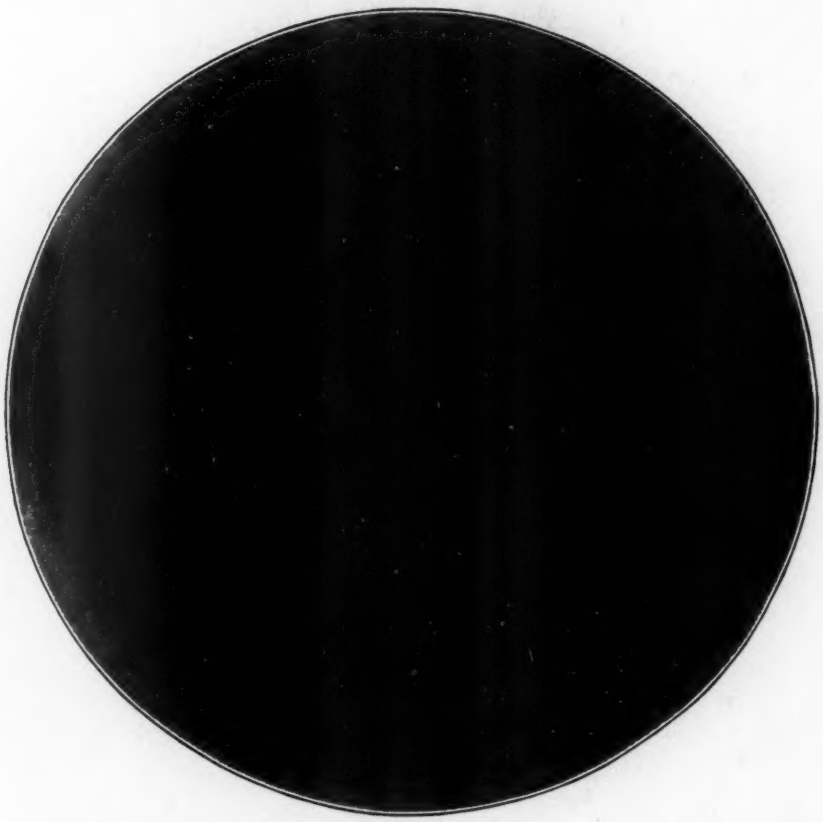

Fig. 4.—Low power photomicrograph of a cross section taken through the normal appearing nerve sectioned near the chiasm.

Roentgenograms of the optic foramens, taken on April 11, as interpreted by Dr. Rolla G. Karshner, revealed a definite enlargement of the right optic canal (fig. 2). Examinations of the urine and blood gave negative results.

First Operation.—In view of the findings, a diagnosis of primary glioma of the right optic nerve in the intraorbital portion with extension toward the chiasm was made. An intracranial exploration was carried out on April 27 by one of us (Dr. Rand), at which time a right frontal craniotomy and section of the nerve about 1 cm. from the chiasm was performed. Both optic nerves were clearly seen. Starting about 1.5 cm. from the chiasm, the right nerve was seen to be symmetri-

cally swollen through the optic foramen. The orbital roof was removed; the nerve was sectioned anterior to the foramen and removed. The osteoplastic flap was then closed in the usual fashion, and the patient was given 200 cc. of whole blood by the multiple syringe method at the conclusion of the procedure. The postoperative course was essentially uneventful.

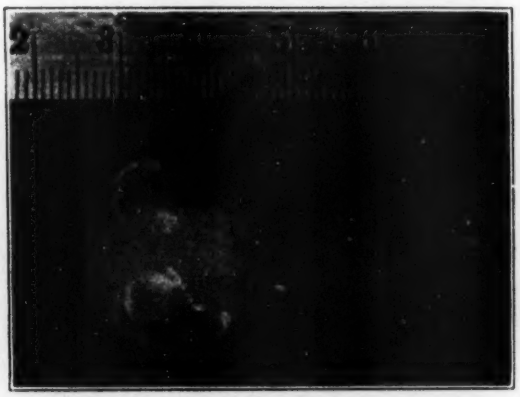

Fig. 5.—Photograph of the eyeball and remaining portion of the optic nerve and tumor attached to the globe, removed on May 24.

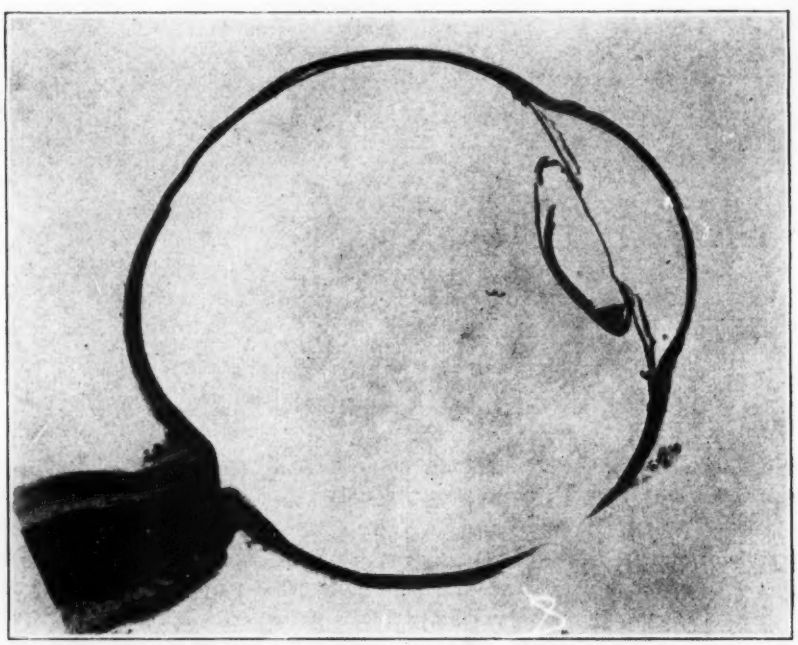

Fig. 6.—Low power photomicrograph of a sagittal section taken through the globe and optic nerve where it enters the globe.

The specimen obtained at the first operative procedure, April 27, consisted of a somewhat fusiform, grayish red enlargement of the optic nerve, measuring 1.3 by 0.8 by 0.5 cm. A solution of formaldehyde was used as a fixative. The orbital

portion was noticeably wider than that removed at a distance of about 1 cm. from the chiasm, where it appeared normal in size. The gliomatous enlargement was smooth and moderately firm, though somewhat elastic in consistency. The dura was not adherent.

Microscopic Examination.—A cross section of the nerve at its widest portion revealed the fascicular pattern of the nerve preserved though greatly accentuated (fig. 3). The pear-shaped spongioblastic cells with their delicate processes were seen to invade not only the nerve fibers but the connective tissue stroma as well. In the region of the septums the blood vessels were often increased and dilated.

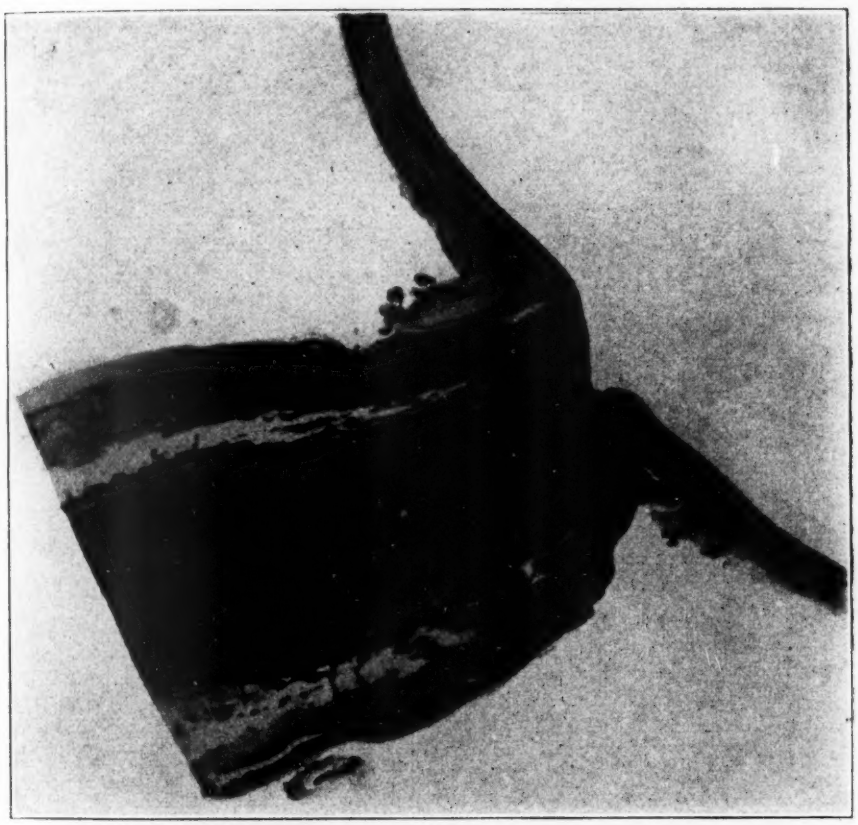

Fig. 7.—Higher magnification of the optic nerve entering the globe showing increase in gliosis but with preservation of normal fasciculi. There is gliosis at one edge of the disk with loss of pigment epithelium for a short distance beyond this edge.

In some places their walls were thickened and hyalinized and gave an angiomatous appearance to the neoplasm. Vacuolation of the cells was evident here and there, leading to the formation of a few small cystic cavities. Some of the cells gave the appearance of being astrocytes, but the polar spongioblastic character of the predominating cell was evident. The only normal nerve tissue remaining was found at the periphery of the section, and this revealed moderate fibrosis of the nerve sheath. A section through the fairly normal appearing narrow por-

tion of the nerve showed a small amount of fibrinous polymorphonuclear exudate at the periphery. There was no evidence of neuroglial proliferation through the nerve fibers or connective tissue stroma (fig. 4). The diagnosis seemed obviously that of primary glioma of the optic nerve, spongioblastic in type.

Second Operation.—Since the greater part of the orbital nerve had not been removed at the first operation and miscroscopic examination had revealed the nature of the tumor, it was decided to remove the globe with the remaining portion of the nerve. This procedure was delayed until healing from the first operation had progressed sufficiently that subsequent enucleation would not be dangerous

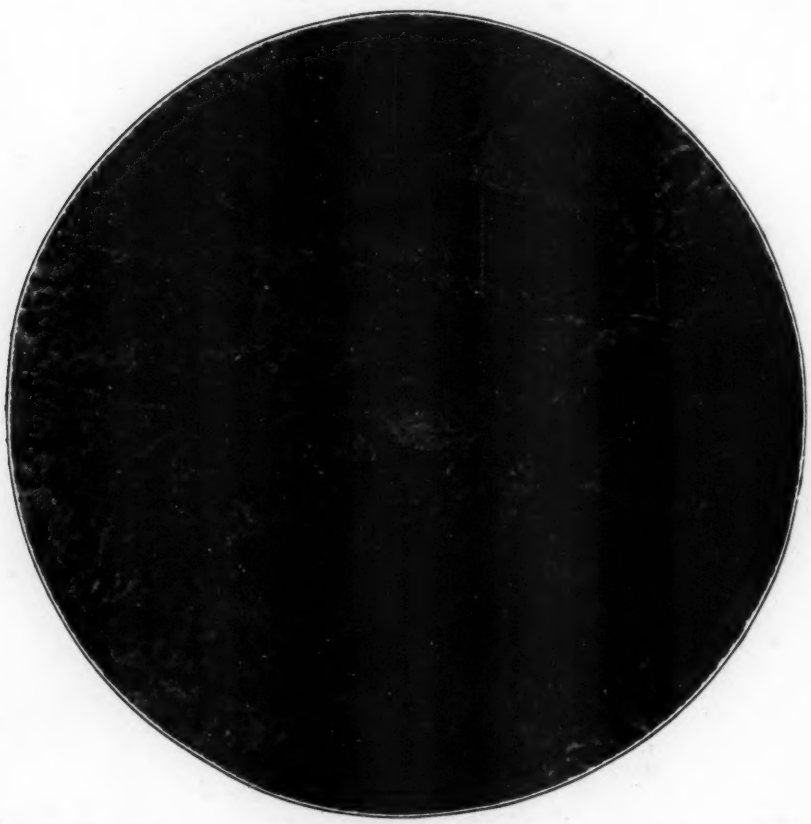

Fig. 8.—High power photomicrograph of detail from figure 7, showing gliosis with preservation of the normal pattern.

from the point of view of infection from the conjunctiva. On May 24 one of us (Dr. Irvine) enucleated the eye with the remaining portion of the nerve attached. The patient made an uneventful recovery and was discharged from the hospital on June 3.

The specimen removed on May 24 consisted of the eyeball and optic nerve (fig. 5). The eyeball appeared normal. The nerve was more or less uniformly dilated, measuring 2.5 cm. in length and 8 mm. in diameter at its widest portion. Except for a sudden constriction to normal size as it entered the sclera, the enlargement of the nerve extended to the globe. Over its entire course the

enlargement was superficially cystic, particularly near the globe. After the globe was fixed in a solution of formaldehyde, it was opened and found to be essentially normal. The retina was in situ, and no gross pathologic process was seen at the disk.

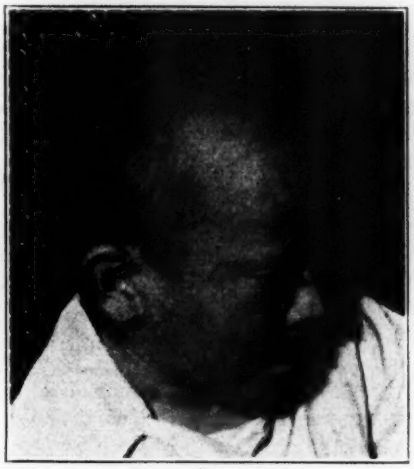

Fig. 9.—Photograph of the patient taken on May 11, fourteen days after intracranial section of the right optic nerve.

Fig. 10.—Photograph of the patient taken on June 1, two days before his discharge from the hospital.

Microscopic Examination.—The pathologic changes were limited to the optic nerve, the eyeball being normal (figs. 6 and 7). The nerve was greatly increased in size. The normal pattern of the nerve was maintained to a great extent, the enlargement being partially due to an increase in neuroglia within the interseptal spaces but for the most part due to marked meningeal reaction.

The outstanding change in the nerve proper was the increase in glial cells (fig. 8). For the most part these varied from round to spindle shape, with a rather clear nucleus containing a nucleolus and rather prominent chromatin. A finely reticulated matrix could be made out, which was more apparent toward the periphery, where there was a suggestion of fine vacuolation in excess of that over the normal neuroglial mantle. Cross section revealed the normal pattern more or less intact and the axis-cylinders present in the periphery. Some of the glial cells were large, approaching a giant cell type.

The leptomeninges were distended by marked proliferative reaction, characterized by a large amount of collagen arranged more or less in parallel thick fibers. Whether or not part of the dense cellular reaction represented proliferation of tumor cells in the vaginal space could not be definitely ascertained but seemed unlikely, as the change in the nerve at this point was rather slight.

The lamina cribrosa curved backward slightly and was questionably thickened as a result of a slight increase in the spindle cells. The optic disk showed some gliosis at one edge, and for a short distance beyond this edge there was a loss of pigment epithelium. The appearance here was somewhat like that of supratraction of the retina due to myopia. A persisting tag of hyaloid artery remained on the disk in some of the sections. The appearance of the disk ophthalmoscopically was undoubtedly the result of the gliosis. The retina appeared normal. The retinal ganglion cells seemed slightly diminished in number.

Slides were sent to Dr. Verhoeff, who confirmed the diagnosis, saying that this was undoubtedly a glioma of the optic nerve such as he has described [2] as the finely reticulated type.

DIAGNOSIS

An intraorbital tumor of the optic nerve can usually be diagnosed with much more certainty than can primary intracranial neoplasm of the nerve. Proptosis and slowly progressive loss of vision are the most common manifestations of an intraorbital tumor. Impairment of vision usually precedes proptosis in cases of glioma, while the reverse is true with endothelioma or fibroma. Because the tumor grows slowly, visual disturbances may begin many years before the onset of proptosis. The direction of displacement of the globe usually coincides with the direction of the orbital axis, but exceptions are noted if the growth becomes large. Limitation of motion of the globe may or may not be present and is more often noted in cases of endothelioma and fibroma than in those of glioma.

Secondary atrophy of the optic nerve is the most common abnormality found on ophthalmoscopic examination. Papilledema may occur with or without evidence of atrophy and is most frequently observed in association with a growth lying close to the globe or in cases in which intracranial pressure is increased.

According to the literature, a normal fundus is occasionally seen in the presence of an intraorbital tumor of the optic nerve. This was noted in 3 of the 118 cases collected by Hudson,[1] the growth in each of the 3 instances being an intraneural glioma. In slightly more than

half of his cases atrophy of the optic nerve was found; the terms optic neuritis and papilledema were used in describing the condition in the remainder.

A roentgenogram of the optic foramen is a most important diagnostic aid in these cases, as the foramen may be considerably enlarged. Without evidence of orbital extension, such as enlargment of the optic foramen and exophthalmos, a diagnosis of primary intracranial glioma of the optic nerve probably can never be made with certainty without surgical exploration. Martin and Cushing [8] were able to diagnose such a tumor preoperatively in only 1 of 7 cases. Atrophy of the optic nerve and slowly progressive loss of vision in one or in both eyes are frequent findings. The visual fields may show bitemporal or homonymous hemianopia, or total blindness in one eye and hemianopia in the other. Roentgenograms may show deformation of the sella turcica and enlargement of one or of both optic foramens. The absence of such evidence, however, is no proof that the lesion may not have extended through the optic foramen, because instances of such extension without deformation of the canal have occurred. Unless the growth becomes large enough to cause an increase in intracranial pressure, papilledema is not produced by a tumor confined to the chiasmal or prechiasmal portion of the optic nerve.

GROSS AND MICROSCOPIC PATHOLOGIC PICTURE

As described by Grinker,[9] the glioma on gross appearance usually has a smooth surface, is somewhat spindle shaped and is covered by easily detached dura. It may, however, appear as a spherical enlargement of the nerve, a solid, irregular thickening along its entire course, or more often as several small nodules separated by thick tubular tissue. Although the dura is rarely penetrated, it may be thinned out and contain tumor tissue on its inner surface. The diameter, of course, is variable, often measuring from 1 to 2.5 cm. The sectioned enlargement discloses either a diffusely thickened optic nerve recognizable as such or an optic nerve peripherally compressed by a grayish red tumor nodule.

Sattler [10] and Verhoeff [2] have shown that when the tumor infiltrates to the papilla it may be visible ophthalmoscopically as a small papillary cyst. Variable-sized cysts filled with mucoid material are not infrequently seen. These cysts, containing a homogeneous substance previously considered mucin, explain the old term myxoma. According

8. Martin, P., and Cushing, H.: Arch. Ophth. **52**:209, 1923.

9. Grinker, R. R.: Tumors of the Optic Nerve, Arch. Ophth. **4**:497 (Oct.) 1930.

10. Sattler, H.: Die bösartigen Geschwülste des Auges, Leipzig, S. Hirzel, 1925.

to Fleischer and Scheerer [11] and Sattler,[10] however, this substance does not stain with mucicarmine or mucihematin. Verhoeff [2] expressed the belief that the cysts which contained serous fluid, small amounts of fibrin and a few red blood cells arise from a fusion of the vacuoles found in the reticulum. Löhlein,[12] on the other hand, was of the opinion that the cysts are the result of areas of degeneration secondary to the marked degenerative and hyaline changes of the walls of the vessels. The cysts may be large. In fact, in Adamuck's [13] case the entire tumor comprised a cyst.

The microscopic appearance of these gliomas created great diversity of opinion among the earlier writers on the subject. They were regarded as mesoblastic, epiblastic, malignant or benign, and again of the nature of a hypertrophy rather than a true new growth. They were referred to by such names as sarcoma, myxosarcoma, glioma, gliomyxosarcoma, adenoma and endothelioma. In 1879 Willemer [14] assembled from the literature the reports of 25 cases in which the most variable histologic structures were described, though many of the growths were doubtless true gliomas of the nerve. In 1892 Sattler [15] expressed the belief that of the essential tumors of the optic nerve, the majority conformed to a type which he called myxofibroma, while only a small portion were endotheliomas.

Hudson [1] in 1912 collected and analyzed all previously reported cases of tumor of the optic nerve. Fortunately, he simplified the classfication by dividing the tumors into three groups: those showing gliomatosis, those showing fibromatosis and those of endothelial origin. The second and third groups, of course, consisted of tumors which arose from the nerve sheath or their meningeal envelops, but the first group, tumors exhibiting glial proliferation, consisted of 118 tumors, the larger number of which had been described as myxosarcomas of one form or another. Interestingly enough, in all but 1 of the 11 cases in which there was a postoperative fatality with subsequent autopsy, an extensive intracranial involvement of the nerves and chiasm, often with more or less invasion of the brain, was the invariable postmortem observation. Moreover, it was evident that in 14 other instances symptomatic evidence of intracranial disease had already appeared by the time the cases were reported.

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11. Fleischer, B., and Scheerer, R.: Arch. f. Ophth. **103**:46, 1920.
12. Löhlein, W.: Arch. f. Ophth. **73**:335, 1914.
13. Adamuck, S.: Arch. f. Augenh. **28**:129, 1894.
14. Willemer, F.: Arch. f. Ophth. **25**:161, 1879.
15. Sattler, H.: Ueber die eigentlichen Sehnerventumoren und ihre chirurgische Behandlung, in Beiträge zur Chirurgie: Festschrift gevidmet Theodor Billroth von seinen dankbaren Schülern, Stuttgart, [Hoffmann], 1892, p. 314.

Byers [16] in his publication of 1914 expressed the belief that tumors growing within the dural sheath could not be separated definitely into two divisions. He pointed out that such growths essentially represented an overgrowth of the fibrous connective tissue elements of the optic nerve and that almost every phase of development, from the embryonic myxomatous type to the fine fibrous bands described by the term fibromatosis, could be found. In the second group of neoplasms he attributed the changes to a proliferation of local endothelial cells and classified the growths as endotheliomas. He further added that the two groups were histogenetically related.

At the present time it seems rather generally conceded that these gliomas of the optic nerve are spongioblastic in type. The similarity of these growths caused Verhoeff [2] to state that there could be little doubt but that they were all of the same nature. The same elements could be seen in all of the tumors but in different proportions and arrangement, and all were primarily composed of neuroglia. Verhoeff [2] classified them into three groups, with transitional forms between either one or both of the other groups. The first group he designated as the finely reticulated type with irregularly running fibrils comprising a matrix for small, oval nucleated cells containing a small amount of feebly staining cytoplasm, frequently vacuolated, a type similar to but not identical with the neuroglia of the normal optic nerves. The second group he called the coarsely reticulated type, which appeared to be an exaggeration of the first, with heavier fibrils, larger intracellular vacuoles and a greater tendency to cystic formation. His last group he designated as the spindle cell, or coarsely fibrillated, type, consisting of coarse neuroglia fibrils, many of which were partly spiral in form, with neuroglial cells lying between them.

Although on occasions the vascularity of these gliomas has been sufficient to have them mistaken temporarily for angiomatous lesions, ordinarily the tumor is not very vascular. Numerous thin-walled, dilated vessels are not infrequently described and are usually found in the septums, the common locality for vascular changes in the optic nerve. Hyaline degeneration of the walls of the blood vessels and secondary hemorrhages within them are not uncommonly noted. Although there is great variation of the pia-arachnoid and the extension of its septums into the nerve, they are usually greatly thickened and composed of irregular masses of collagenous tissue into which glia fibers have grown in all directions.

Occasionally a myelin sheath may persist, and small, normal appearing bundles of axis-cylinders appear intact in the peripherally com-

16. Byers, W. G. M.: Tumors of the Optic Nerve, J. A. M. A. **63**:20 (July 4) 1914.

pressed remnant of the optic nerves, but usually the optic nerve fibers are spread apart by the tumor and demyelinated early.

Whether the growth is intraorbital or intracranial, the descriptions of fundamental cell type have been generally similar. The cells are fairly long and spindle shaped, with oval nuclei and processes arising from each end. Sattler [10] described them as oval cells with corkscrew-like processes; Sourdille,[17] as bipolar cells with two prolongations, and Favaloro,[18] as bipolar fusiform cells with short, broad expansions, forming a syncytium.

Verhoeff [2] first described as cytoid bodies rounded or elongated hyaline masses. The largest may attain a cross diameter of 0.025 mm., and they may reach a length of 0.10 mm. None of the bodies contained definite nuclei, although occasionally, after staining with alum hematoxylin, some resemblance to a nucleus was produced by a portion of the substance staining more deeply than the rest. These pseudonuclei never showed nuclear membranes or contained chromatin nets or nucleoli. Continuous from them in a few instances were long processes which could be followed into a spindle-shaped neuroglial cell. Verhoeff was of the opinion that they were atypical or giant neuroglial fibers. Martin and Cushing,[8] on the other hand, considered them merely masses of coalesced glial fibers.

According to Grinker,[9] these tumors contained numerous mitotic figures, but Verhoeff [2] has never found any neuroglial nuclei undergoing either direct or indirect division. He accounted for this on the basis of the slow rate of proliferation.

Favaloro [18] found small round cells without processes and with two or more nuclei, which he considered to be oligodendroglia. He also discovered astrocytes mixed with bipolar fusiform cells. Enriquez [19] and Marchesani [20] reported astrocytes and oligodendroglia in the normal optic nerve, but at the present time no definite differentiation of the spongioblasts into the more advanced glia cells has been reported in tumors of the optic nerve.

As the optic nerve contains all of the adult forms of neuroglia, it is not unreasonable in gliomatous tumors of this nerve to expect characteristics and differences in malignancy similar to those found in cerebral gliomas. The fact that at the present time these tumors have invariably been reported as spongioblastic does not, of course, mean that other gliomatous types will not be found subsequently. It is to be remembered, however, that certain of the gliomas are discovered more

17. Sourdille, G.: Arch. d'opht. **24**:87, 1904.
18. Favaloro, G.: Ann. di ottal. e clin. ocul. **56**:619, 1928.
19. Enriquez, L.: Bol. Soc. españ. de hist. nat. **26**:1, 1926.
20. Marchesani, O.: Arch. f. Ophth. **117**:575, 1926.

often in some localities of the brain than in others. Thus the polar spongioblastoma predominates in the region of the third ventricle, optic chiasm and optic nerves, while the medulloblastoma is most commonly found in the central cerebellar region of children, and the glioblastoma multiforme, preeminently the glioma of adult life, occurs almost invariably in the cerebral hemispheres. For this reason one could scarcely be surprised if the polar spongioblastoma were the glioma of the optic nerve and chiasm invariably found.

As these gliomas of the optic nerve are seen much less frequently than cerebral gliomas and facilities for the specific staining methods are not always available, it is not surprising that a satisfactory understanding of their classification and variation in malignancy has not been obtained. Even though various spongioblastic tumors may appear similar, differences in rapidity of growth in the group is to be expected, just as in the different groups of cerebral gliomas.

TREATMENT

Complete surgical removal of the involved nerve offers the best prognosis for preservation of life and vision. As emphasized by Dandy,[7] the fact that a high percentage of intraorbital tumors of the optic nerve extend into the cranial chamber increases the surgeon's responsibility in determining whether or not there is intracranial extension before he is content with orbital removal. Unfortunately this often cannot be determined with satisfaction preoperatively. Enlargement of the suspected optic foramen would seem sufficient evidence to justify the assumption that the tumor has invaded the intracranial portion of the nerve, although, as mentioned previously, absence of such enlargement is no proof that this has not occurred. Should local enucleation be done, a section of the cut nerve should be studied to determine if possible whether or not all the tumor has been removed. If central extension is found, intracranial removal of the entire nerve is advisable. To minimize the chance of ensuing meningitis, this should be postponed until complete healing has occurred after the orbital operation. Experience shows that meningitis frequently occurs when craniotomy and enucleation are performed too close together. Even without subsequent craniotomy, the danger of meningitis following the orbital approach is noteworthy. Verhoeff [2] observed that meningitis occurred in about 10 per cent of Hudson's cases when the orbital approach was the only procedure used. The danger appeared particularly great with intracranial involvement of the nerve, for in 10 of the 11 cases of meningitis such intracranial extension was found at autopsy.

As has been mentioned by Verhoeff,[2] in intraorbital operations it seems advisable to remove the eye with the tumor. This permits use of an artificial eye and affords a satisfactory cosmetic result. When the

tumor is removed without the globe, there may result an unsightly strabismus or ptosis, and, because of degenerative changes, the eye may ultimately require removal. However, Knapp [21] and Weskamp [22] have advocated preservation of the eye following a Krönlein procedure for removal of an intraorbital glioma. Knapp [23] says that 4 patients operated on by him by the Krönlein method have been followed now for fifteen to twenty years, and the eye remains perfectly normal in appearance and no intracranial disturbance has developed, in spite of the fact that 3 of these patients showed roentgen evidence of enlargement of the optic canal. Weskamp reported a case in which one and a half years after this method was used the patient's eye was in excellent condition in spite of sectioning of the central vessels and ciliary nerves.

Because complete removal of the glioma of the optic nerve with sufficient normal nerve affords the greatest chance of cure, in a healthy young person the intracranial procedure with unroofing of the orbit and section of the nerve distally and proximally to the globe in many ways seems the procedure of choice. Adequate dural closure prevents leakage of the cerebrospinal fluid and, from the standpoint of meningitis, makes subsequent enucleation less precarious.

Although the intracranial procedure is more hazardous from an operative point of view, in experienced hands the mortality rate is not high. Meningitis is less likely to occur than with the orbital approach, and much more certain determination of the extent of the neoplastic growth can be obtained. Some of the intraorbital gliomas of the optic nerve even extend so close to the optic foramen that complete intraorbital removal is impossible.

PROGNOSIS

The prognosis for these neoplasms depends on the location and extent of the growth as well as on the degree of malignancy. After complete removal of an intraorbital tumor, the possibility of recurrence in the orbit is remote. DeLong [3] stated that recurrence under such circumstances has never been reported.

In view of the fact that in many cases removal has been incomplete and yet no case has been reported in which there has been recurrence of the tumor in the orbit, Verhoeff [2] suggested that perhaps excision of the largest part of the tumor might in some way eliminate a stimulating factor or substance, thus inhibiting further extension of the growth. Experience with similar types of cerebral tumors fails to support such a supposition. Moreover, the rarity of glioma of the optic nerve scarcely

21. Knapp, A.: Contributions to Ophthalmic Science, Menasha, Wis., George Banta Publishing Company, 1926.

22. Weskamp, C.: Glioma of the Optic Nerve: Report of a Case, Arch. Ophth. **13**:630 (April) 1935.

23. Knapp, A.: Personal communication to the author.

allows a proper evaluation of this point of view. The fact that some of these tumors, as in the case here reported, have grown fairly rapidly within a period of several months makes one realize that incomplete removal would be hazardous and unjustifiable even though, in contrast to retinal gliomas, recurrence would be slow. Furthermore, although a partially extirpated tumor may not recur in the orbital tissues, there is no evidence that subsequent slow extension along the nerve to the brain is inhibited by partial removal.

Should the tumor involve the chiasm, there is little to be accomplished surgically or otherwise. Three of the 7 persons operated on by Dr. Cushing [8] died within forty-eight hours after operation, and in no instance was any beneficial result obtained. As mentioned by Grinker,[9] death with hyperpyrexia not infrequently occurs from manipulation of the chiasmal gliomas, probably as a result of disturbance of the heat-regulating center at the base of the brain behind the chiasm. Mehney's [24] recent report of 3 cases of glioma of the optic nerve from Peet's clinic included 1 in which the growth had extended into the chiasm. The patient died twenty-four hours postoperatively with hyperpyrexia.

It was the opinion of Martin and Cushing [8] that should clinical diagnosis of extension into the chiasm be sufficiently perfected, there would be every reason to avoid operation, although in case of doubt exploration would have to be carried out. High voltage roentgen therapy has been tried in these cases but has proved of little if any significant benefit.

SUMMARY AND CONCLUSIONS

Glioma of the optic nerve is rare, less than 300 cases having been reported. Seventy-five per cent occur in the first decade of life. In a high proportion of cases there is extension of the tumor into the cranial cavity.

A case is presented with the clinical and pathologic observations.

The suggestive diagnostic signs are the ophthalmoscopic appearance of atrophy of the optic nerve or optic neuritis, slowly progressive nonpulsatile exophthalmos and enlargement of the optic foramen, as seen roentgenographically.

The polar spongioblastoma is the invariable type of glioma found involving primarily the optic nerve. Since, from an embryologic standpoint, the optic nerve contains all the adult forms of neuroglia, it is logical to presume that advanced glial tumors will be reported in the future as more of these neoplasms are discovered and studied with differential staining methods.

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24. Mehney, G. H.: Primary Tumor of the Optic Nerve: Report of Three Cases, Arch. Ophth. **16**:95 (July) 1936.

Intracranial extension of glioma of the optic nerve occurs more frequently than is usually appreciated, as judged by the prevailing attitude of the ophthalmic literature regarding treatment of these growths. The unjustifiable hazard involved when the surgeon is content with incomplete orbital removal is not sufficiently realized.

A glioma of the optic nerve usually grows slowly, and orbital recurrence, even after incomplete orbital removal, has not been reported. In spite of this fact, however, extension along the proximal nerve to the optic chiasm may occur and implies a fatal prognosis. If such extension is to be prevented, complete removal of the involved nerve is necessary. Technically, complete extirpation is more certain and meningitis less likely to occur if done through the intracranial approach. Considering the incidence of meningitis following the orbital approach, the intracranial approach cannot be considered a radical procedure, since it minimizes the possibility of meningitis.

Roentgenograms of the optic foramen should be made in all cases in which a tumor is suspected. The finding of an enlarged optic foramen is specific indication for intracranial section of the nerve with removal of the intraorbital portion of the nerve at the same time.

When there is clinical evidence of intracranial extension, early intraorbital removal of the involved nerve is recommended. If all the tumor tissue has been removed, further operation is not indicated. Should invasion of the stump by neoplastic tissue be found, intracranial section of the optic nerve at the chiasm and entire removal of the stump should be carried out.

THE PRODUCTION OF CORNEAL ULCERS IN THE RABBIT

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PHILADELPHIA

Previous attempts to produce a standardized corneal ulcer in the rabbit have been unsatisfactory. Bach [1] in 1894 was the first to attempt the production of a corneal ulcer for the purpose of evaluating specific treatment. He was not able to obtain uniformity, nor was Key [2] or Bursuk.[3] Brown and Pugh [4] finally succeeded in producing a fairly satisfactory ulcer by using a strain of staphylococcus which they found only after many trials. Most strains gave either too much inflammatory reaction or none at all. No mention is made in their paper of the production of hemolysin or pigment by their strain.

Strumia and Scarlett [5] in 1936 succeeded in obtaining a consistent keratoconjunctivitis for their study of the therapeutic effect of specific bacteriophage. They were able to get consistent infection only by giving intradermal injections of heat-killed staphylococci for three days previous to the injection of live organisms into the cornea. This

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* Fellow in Ophthalmology.

Read at the Section on Ophthalmology of the College of Physicians, Philadelphia, Dec. 15, 1938.

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1. Bach, L.: Experimental Investigations on the Staphylococcus Ulcer of the Cornea and Its Therapeutics, Cong. période. internat. d'opht., Compt. rend. **8**:133, 1894.

2. Key, B. W.: Influence of Protein Therapy on Experimental Staphylococcic Infection of the Rabbit's Cornea, Am. J. Ophth. **9**:351, 1926.

3. Bursuk, G. G.: Therapeutic Immunization with Immunogen B (Staphylococcic Vaccine) in Experimental Ulcer, Vestnik oftal. **10**:517, 1937.

4. Brown, A. L., and Pugh, J.: Effect of Intraocular Concentration of Typhoid Antibodies on Experimental Corneal Ulcers, with Report of Seven Cases, Arch. Ophth. **16**:476 (Sept.) 1936.

5. Strumia, M. M., and Scarlett, H. W.: Effect of Bacterial Lysate on Staphylococcic Keratoconjunctivitis in Rabbits, Arch. Ophth. **15**:47 (Jan.) 1936.

procedure was based on the work of Julianelle and his co-workers.[6] The latter investigators, however, used scarification of the cornea in their experiments on sensitivity. Strumia and Scarlett found that injection into the cornea gave more consistent results. Julianelle and his co-workers observed that weekly instillations of an extract of staphylococci into the scarified area were necessary for at least four weeks before a reaction could be obtained. The short period of sensitization with heat-killed staphylococci, which was found by Strumia and Scarlett and confirmed by us, is explainable on the assumption that sufficient antibodies were stimulated to give an antigen-antibody reaction in the cornea and thus limit the infection to a corneal ulcer.

Circulating antibodies are not usually detectable before the sixth day. From a week to ten days is required before a guinea pig is sensitized to horse serum sufficiently to show the usual systemic manifestations of sensitivity. It may be that the corneal reaction is a delicate test for the presence of specific antibodies; further investigation of this is desirable. The formation of antibodies in general is dependent on the amount of antigen given and the frequency of the dose. Too much antigen may inhibit the reaction in certain instances.

Brown and Pugh reported that typhoid antibodies appeared in the blood in small quantities (a titer of from 1:5 to 1:20) within from twenty-four to forty-eight hours after intravenous injection of a suspension of 10,000,000 killed organisms. The titer rises from this time onward, and if no subsequent dose is given, reaches its height on about the sixteenth day. According to the authors, the ocular vessels in the normal eye are impermeable to agglutinins, and a relatively low titer of the aqueous (1:2 or less) persists even in the presence of a rising titer of the serum. The titer of the aqueous was increased, however, by aspiration of the anterior chamber.

The present investigation is an attempt to produce a corneal ulcer which would be accompanied by a minimum amount of conjunctival reaction but would still show staining with fluorescein and infiltration of the cornea for at least ten days. We were fortunate to be able to obtain the original strain of staphylococci used in the experiments of Drs. Strumia and Scarlett.

EXPERIMENTAL METHOD

A six hour subculture of this original strain in neopeptone broth was used for the first corneal injection. On the following day material was obtained from the right eye of the rabbit and spread on a 5 per cent rabbit blood agar plate. After

6. Julianelle, L. A.; Morris, M. C., and Harrison, R. W.: An Experimental Study of Corneal Vascularization, Am. J. Ophth. **16**:962, 1933.

twenty-four hours at 37 C. the plate showed two types of colonies; one was yellow and hemolytic and the other, white and nonhemolytic. Each type was spread separately on a 5 per cent blood agar plate for isolation. Staining of both cultures with Gram's stain showed pure colonies of gram-positive cocci in clusters. After eighteen hours' growth at 37 C. subcultures of the albus strain were made in 0.5 per cent dextrose neopeptone broth. The albus strain was chosen for further work, because the aureus strain produced too much reaction. It is well known that Staphylococcus aureus haemolyticus is much more pathogenic [7] than the nonhemolytic albus strains. These were centrifuged after eighteen hours' incubation, the supernatant fluid was discarded and the sediment was suspended in 0.85 per cent solution of sodium chloride and heated at 60 C. for forty minutes. One loopful planted in broth showed no growth in eighteen hours. This suspension containing 4,000,000 heat-killed staphylococci per cubic centimeter was used for subsequent subcutaneous injection. It was stored without preservative in a refrigerator in a vial stoppered with rubber; required amounts were withdrawn by needle and syringe under sterile precautions.

The amount of antigen used in our experiments, which was 0.1 cc. of the suspension of heat-killed white staphylococci given subcutaneously each day for three days, followed by the injection of living staphylococci into the cornea on the fourth day, is within the usual limits of ordinary experimental procedure. No tests were made on the blood to determine the presence of circulating antibodies.

The corneal injections were made with eighteen hour subcultures of the nonhemolytic white organisms in 0.5 per cent dextrose neopeptone broth. Each culture was examined by Gram's stain for purity before injection. Thirty rabbits (60 eyes) were used in this investigation. Anesthesia was obtained with 2 drops of a 0.5 per cent solution of pontocaine hydrochloride. A 26 gage short beveled needle was used, and 0.05 cc. of the broth culture was injected intracorneally about 2 mm. from the limbus, care being taken to keep the point of the needle from entering the anterior chamber. Occasionally some of the culture leaked out around the needle, but this did not seem to affect the final result.

The animals were observed for the following criteria: secretion, corneal infiltrate, staining, hypopyon and the formation and regression of pannus.

RESULTS

The most constant factor seen in the animals was the appearance of pannus on the fourth or the fifth day. It usually appeared as a heavy brush of vessels from the limbus nearest the site of the ulcer; occasionally it appeared as a typical "salmon patch." This is without doubt the pannus of infection described by Julianelle and his co-workers, as it was definitely related to the severity of the infection. The ulcer did not begin to improve until the pannus appeared.

The ulcers produced were accompanied by a moderate conjunctival reaction and secretion. This reaction subsided gradually after the third day and was the type that might be expected with any pyogenic corneal ulcer. The cornea was hazy within twenty-four hours, the

7. Chapman, G. H.; Berens, C.; Nilson, E. L., and Curcio, L. G.: Differentiation of Pathogenic Staphylococci from Nonpathogenic Types, J. Bact. **35**:311, 1938.

hazing increasing slightly till about the third day and then remaining about the same until the ulcer began to heal on about the seventh or the eighth day. Staining with fluorescein was present until the haze had practically disappeared. The ulcers usually measured from 2 to 3 mm. in diameter and involved the superficial layers of the substantia propria. They healed completely, leaving only a faint nebula and empty vessels at the end of three weeks. When the opposite eyes of the first 12 rabbits were inoculated about three weeks after the original injection, no difference in the duration and severity of the ulcers from that in the first eyes was noted. The most uniform results were obtained when both eyes of 8 rabbits were inoculated at the same time. The severity of the infection varied to some extent for each individual of the species, but there was marked uniformity in the appearance and course of the two eyes when they were inoculated at the same time. Six rabbits that were not sensitized to specific vaccine showed more variation than those that had been sensitized, though the two eyes of each animal were remarkably similar. The variation observed in the nonsensitized rabbits was either toward more extensive involvement of the eye or toward a minimal reaction; approximately half of the eyes cleared completely in from three to four days without treatment, while in 2 of the rabbits hypopyon ulcers developed accompanied by a fairly severe reaction. The 8 eyes into which dead organisms were injected showed slight conjunctival reaction in twenty-four hours; the cornea of each eye was clear but stained at the site of the injection. Within forty-eight hours all that remained was a faint nebula, which practically disappeared in four days. No pannus was observed in any of these rabbits.

Hypopyon ulcers were produced in 4 eyes. This was a complication that we tried to avoid. It occurred early in our series when we were perhaps less skilful in our technic and twice in the last series when the animals were not sensitized.

Some of the ulcers were treated when we observed that a consistent ulcer was being obtained. Five eyes were irradiated with grenz rays (in varying doses). We realized at the time that this type of treatment might not be satisfactory, since the ulcers were fairly deep. The results in this small series were not significant. Sixteen eyes were treated with subconjunctival injections of Pregl's solution (a complex aqueous solution containing 3 per cent of available iodine); 0.5 cc. was injected every day for three days, starting twenty-four hours after the corneal injections. Though every ulcer did not respond to this treatment, the average duration of secretion, hazing and staining was noticeably less than in the eyes that were not treated (fig. 2).

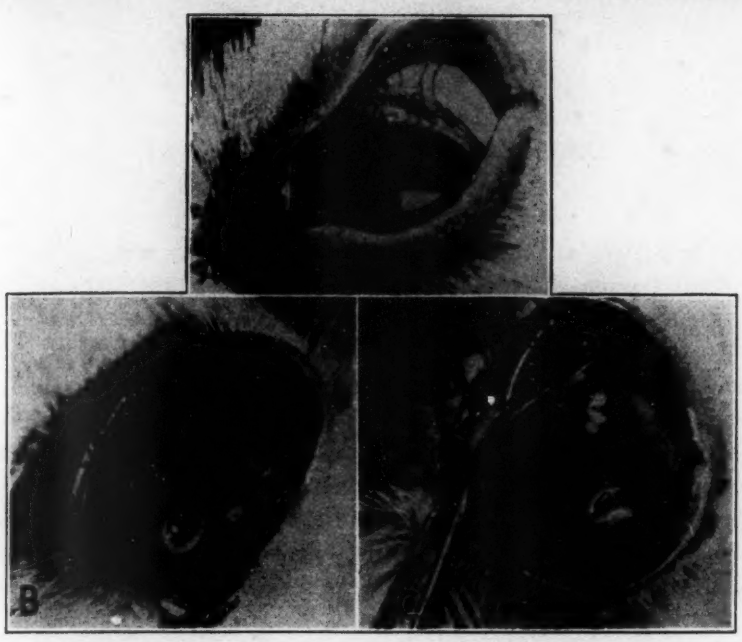

Fig. 1.—*A*, typical pannus formation extending to the site of the ulcer. *B*, ulcer after staining with fluorescein. The staining slightly exaggerates the loss of substance. *C*, early pannus forming at the limbus, hazing of the cornea and circumscribed ulcer.

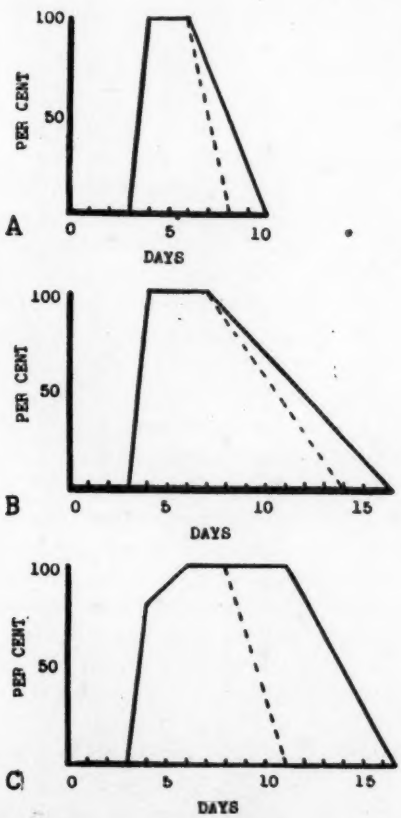

Fig. 2.—*A*, duration and course of corneal secretion. *B*, duration and course of staining of the cornea. *C*, duration and course of corneal infiltration. The ordinates represent the percentage of involvement; i. e., 100 per cent equals maximum reaction. The abscissas represent the time in days. The corneal injections were made after three days of sensitization to a specific vaccine. The dotted lines represent the course of the reaction in the treated animals as compared to that in the animals that were not treated (solid lines).

COMMENT

We feel that a fairly standard staphylococcic ulcer suitable for experimental purposes can be obtained, providing one uses rabbits of approximately the same size and weight and sensitizes them with a vaccine of the same strain that is used to produce the ulcer. When one uses a nonhemolytic nonpigment-forming strain of staphylococci, one can obtain an ulcer that has a minimum amount of conjunctival reaction but will show infiltration and staining of the cornea for approximately from ten to twelve days. When injections are made into both eyes at the same time, there is marked uniformity in the appearance and course of the two ulcers. We suggest that this procedure be carried out when one eye is to be treated and the other used as a control.

SUMMARY

Standard corneal ulcers were produced by injecting living Staph. albus into the corneas of rabbits previously sensitized by subcutaneous injection of specific heat-killed vaccine.

CONGENITAL FAMILIAL EXTERNAL OPHTHALMOPLEGIA WITHOUT PTOSIS

WITH A LESION OF THE PYRAMIDAL TRACT

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Congenital disturbances of the ocular muscles occur in the following order of frequency: (*a*) ptosis, (*b*) paralysis of the abducens nerve with or without involvement of the facial nerve and (*c*) complete or incomplete involvement of the third nerve with ptosis. Congenital familial external ophthalmoplegia without ptosis is rare.[1] A case of this anomaly associated with involvement of the right side of the pyramidal tract is reported. The interest in this case lies not only in the rarity of the condition but in the clinical data, which point to a better understanding of the etiology of such anomalies.

A. H., a woman aged 22, was admitted to the neurologic clinic of the New York Post-Graduate Medical School and Hospital complaining of "nervousness," a feeling of tension and "generalized fatigability."

The family history revealed that the patient's grandmother was supposed to have been afflicted with "eye trouble." Persons would remark that she constantly moved her head from side to side when she wanted to observe an object. She could not move her eyes voluntarily. The patient's sister also had similar trouble with her eyes. She could not move them; they were "absolutely stationary." However, she died of sarcoma of the stomach at the age of 21.

The patient's past history was essentially unimportant. Her birth was normal, and she was breast fed. She began to walk at 1 year of age and to talk at 16 months. She had measles at 2 years of age and scarlet fever at 6. Her mother, whose intelligence was limited, stated that she noticed the patient's eyes did not turn when the child was about 2 years of age.

On examination the patient seemed alert and bright looking but had a fixed stare. Her head moved about constantly in all directions, giving one the impression of a restless wandering movement. Her gait was normal, and the associated movements were within normal limits. There were fine horizontal tremors of the outstretched hands; they were not accentuated on intention. The muscular system throughout the body revealed normal strength, and there was no atrophy and no fibrillation. All the deep reflexes of the upper and lower extremities were equal but slightly hyperactive. The abdominal reflexes, both the upper and

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From the neurologic clinic of the New York Post-Graduate Medical School and Hospital.

1. Ulrich, O., in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1933, vol. 16, p. 145.

the lower, were present but unequal; those on the right were diminished. There was an equivocal Babinski sign on the right and positive Oppenheim and Gordon signs on the right. The sensory examination for all modalities revealed normal findings. The ocular examination, which was checked in the ophthalmic department of the hospital, revealed the following data: Vision was 21/100 in the right eye and 20/40 in the left eye. The levator palpebrae muscles showed good function. When the patient attempted to look upward she overacted the frontalis muscles, but her eyes did not move. There was bilateral ophthalmoplegia externa. Slight bilateral external rotation was retained. The pupils were equal and reacted to light and in accommodation. There was no convergence. There was a constant oscillation of the eyes as seen with the ophthalmoscope. All the other cranial nerves were normal.

Roentgen examination of the skull showed no gross abnormality in the detail of the outline of the bones of the vault or of the base. The bones of the vault were within normal limits of developmental variation. There was perhaps an increase in the structural density along the left supraorbital ridge.

The sella turcica was slightly small but nevertheless was within 10 per cent of the normal developmental variation. It was smooth in contour, with no discernible evidence of erosion or pressure atrophy. Neither was there any evidence of such changes elsewhere.

There were small calcific flecks in the region of the frontal bones in the midline.

The accessory sinuses and mastoids showed fair transillumination.

The Wassermann reaction was negative, and the basal metabolic rate was average normal.

COMMENT

Various theories have been advanced to explain these anomalies. The circulatory theory [2] ascribed the etiologic cause to a hemorrhage in the sheaths of the orbital nerves or in the brain itself. This insult most usually occurs during birth trauma. The neurogenic theory [3] was first advocated by Mobius. This placed the lesion centrally as a slowly degenerative process in the nuclei of the motor nerves of the eye. Mobius thought it to be an infantile nuclear atrophy. This, of course, presupposed the presence of an influencing factor in the nuclei which caused it gradually to become atrophic. This explanation was further strengthened by the fact that minimal excursions were always present.[4] With further study of these anomalies and with reports of postmortem

2. Oppenheim, H.: Text-Book of Nervous Diseases, ed. 5, translated by A. Bruce, New York, G. E. Stechart & Co., 1911, vol. 2, p. 1041.

3. Bernheimer, S.: Aetiologie und pathologischen Anatomie der Augenmuskellähmungen, in von Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, Leipzig, Wilhelm Engelmann, 1907, p. 34. Langdon, H. W., and Cadwalader, W. B.: Chronic Progressive External Ophthalmoplegia, Brain **51**:321, 1928. Mobius, P. J.: Ueber infantilen Kernschwund, München. med. Wchnschr. **39**:17 (Jan. 12) 1892.

4. Li, T. M.: Congenital Total Bilateral Ophthalmoplegia, Am. J. Ophth. **6**:817, 1928.

observations,[5] the conception of the nature of the lesion varied. Autopsy did not disclose any degenerative process but merely a defect in the number of cells in the nuclei as well as reduced neural elements in the other motor systems, such as the pyramidal tract, the substantia reticulata and the olives. The fact that patients with ocular anomalies presented other structural abnormalities of the body also added difficulty to the acceptance of the theory of infantile nuclear atrophy.

The muscular theory [6] advocated primary atrophy of the muscles in the eye with secondary retrograde degeneration in the nuclei. Fuchs [7] excised pieces of the levator palpebrae muscle and found thinning of the fibers and degeneration of the sarcolemma. This theory could not adequately explain the ocular defect, so de Schweinitz [8] was led to attribute it to a combination of nuclear defects with a developmental defect in the muscle. Zappert [9] attributed the cause to traumatic injury at birth of the nerves which supply the ocular muscles, with retrograde degeneration of the nuclei.

While some authors have attempted to rationalize along Vogt's theory of pathoclisis [10] or the theory of defects of the segmental anlage,[11] the most important contribution to this question has been derived from studies in embryology. The embryopathophysiologic theory explains the ocular disturbances in these cases. It not only is supported by clinical data but can be verified by experimental procedures. By exposing a definite mouse strain to roentgen irradiation, Bagg [12] produced anomalies of the eyes and the extremities. These were described by him as being

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5. Spatz, H., and Ullrich, O.: Klinischer und anatomischer Beitrag zu den angenborenen Beweglichkeitsdefekten im Hirnnervenbereich, Ztschr. f. Kinderh. **51**:579, 1931.

6. Gourfein, D.: Un cas de double ophthalmoplegie extérieure congénitale et hereditaire chez six membres de la même famille, Rev. méd. de la Suisse Rom. **16**:673, 1896. Bradburne, A. A.: Hereditary Ophthalmoplegia in Five Generations, Tr. Ophth. Soc. U. Kingdom **32**:142, 1912. Lawford, J. B.: Congenital Hereditary Defect of Ocular Movements, ibid. **8**:262, 1888.

7. Fuchs, E.: Ueber isolierte doppelseitige Ptosis, Arch. f. Ophth. **36**:234, 1890.

8. de Schweinitz, G. E.: Complete Bilateral Congenital Exterior Ophthalmoplegia and Double Ptosis; Bilateral Cerebral Cortical Atrophy of the Frontal and Parietal Regions (Encephalograms); Clinical Communication, Arch. Ophth. **5**:15 (Jan.) 1931.

9. Zappert, J.: Ueber infantilen Kernschwund, Ergebn. d. inn. Med. u. Kinderh. **5**:305, 1910.

10. Vogt, O.: Der Begriff der Pathoklise, J. f. Psychol. u. Neurol. **31**:245, 1925.

11. Bauman, G. I.: Absence of the Cervical Spine: Klippel-Feil Syndrome, J. A. M. A. **98**:129 (Jan. 9) 1932.

12. Bagg, H. J.: Disturbances in Mammalian Development Produced by Radium Emanation, Am. J. Anat. **30**:133, 1922.

recessively inherited. They were produced by the formation of a bleb at the anlage of the eyes and of the extremities. The ocular abnormalities represented a constant finding in all of the experiments. Bagg and Little [13] continued these experiments and found the origin of these blebs. They showed that in all embryos of about 8 mm. a clear fluid is expelled through an anterior foramen situated on the roof of the myelencephalon. This fluid is expelled in order to release the internal pressure of the medullary tube, as the latter is in the process of folding on itself.[14] The anterior foramen exists for a short time, between 7 and 10 mm. of embryonic growth. It is then pulled into the anterior part of the fourth ventricle. Its function is taken over by the foramen Magendi, which is formed posterior to the choroidal plexus.

The expressed clear fluid lies on the dorsal surface underneath the integument. Normally, the fluid is driven along mechanically by the elasticity of the epidermis along the concavity of the surface. When there is an abnormal amount of fluid or when there is a hindrance in its path and the bleb is enlarged, there is interference in the embryonic anlage. A prolonged delay at the flexure or ridge may cause an irritation of the capillary bed, and the bleb may be filled with blood. Bennevi [15] stated that "in living embryos I have often observed blood capillaries to burst at the bottom of a clear bleb, and pour the bloody contents into the cellular bleb." The clear bleb and occasionally the bloody bleb may be absorbed, but the abnormally delayed bleb produces typical abnormalities of the eyes and the extremities.

The nuclei of the motor nerves to the eye are all situated at the crucial encephalic flexure in the human embryo. At 7 mm. of embryonic growth the end of the neural tube is bent sharply in the region of the midbrain, so that the axis of the forebrain forms a right angle with the axis of the hindbrain. As the brain bends, the intramedullary canal becomes constricted into the isthmus, thus increasing its inner pressure.[16] It is at this point that an abnormally large bleb may be retained and later filled with blood. The pressure of the bleb on the relatively superficial nuclei produces the defect in the anlage of those tissues.

The foregoing phenomenon explains the occurrence of complete and partial ophthalmoplegia. The nucleus of the third nerve is made up of

13. Bagg, H. J., and Little, C. C.: Hereditary Structural Defects in the Descendants of Mice Exposed to Roentgen-Ray Irradiation, Am. J. Anat. **33**:119, 1924.

14. Keegan, J. J.: Comparative Study of the Roof of the Fourth Ventricle, Anat. Rec. **2**:379, 1917.

15. Bennevi, K.: Embryological Analysis of Gene Manifestations in Little and Bagg's Abnormal Mouse Tribe, J. Exper. Zoöl. **67**:443, 1934.

16. Weed, L. H.: The Development of the Cerebrospinal Spaces in Pig and in Man, Publication 225, Carnegie Institution of Washington, 1917.

groups of ganglion cells extending along the axis of the aqueduct. An injury to any of the groups of these cells might produce a change in the clinical symptoms. It is interesting to note that the nuclei of the levator muscles of the eyelids are placed most cephalad. A lesion which does not extend the entire length of the nuclei would spare the function of these muscles.

The involvement of the right side of the pyramidal tract in the case reported becomes intelligible in the light of the experiments of Bagg and Little. These authors constantly found the occurrence of ocular anomalies together with deformities of the extremities, for the abnormal bleb was usually retained on the dorsal side of the organism and nearly always around the anlage of the eyes and the extremities. It is also plausible that a mechanical hindrance in the form of an abnormal bleb situated at the cephalic flexure might injure the anlage of the motor tract and spare the sensory system. These interferences usually occur in embryos of about 7 or 8 mm., or at the fourth or fifth week of embryonic life, at which time the sensory anlage is already ripened and is therefore more resistant to pressure.

SUMMARY

A case of congenital familial external ophthalmoplegia without ptosis and with signs referable to involvement of the pyramidal tract has been described.

Various theories to account for these anomalies have been studied.

The pathophysiologic disturbance in embryonic development fully explains such findings.

BILATERAL IRITIS COMPLICATING SERUM SICKNESS

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AND
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The usual manifestations of serum sickness are common and are universally recognized. Even relapses, which occur from time to time after free intervals, are well known. Focal reactions in the course of serum sickness, however, are much rarer. The most common type is paralysis due to neurologic disturbances, of which about 100 cases have been reported.[1] Ocular involvement in serum sickness has apparently been the subject of only three contributions, two of which deal with optic neuritis and the third with edema of the retina.[2] The first was that of Mason,[3] who in 1922 described 3 cases in which measurable blurring of the optic disks developed during serum sickness. Two of the patients had received antipneumococcus serum, while the third had been given antimeningococcus serum. A gradual return to normal occurred. In another report Brown [4] in 1925 observed that of 75 persons receiving diphtheria antitoxin, a measurable elevation of the disks and edema of the retina developed in about 20 per cent in from two to three hours after administration of the serum. This subsided shortly, only to return a week later when serum sickness had developed. The amount of involvement of the optic nerve, which in 10 per cent of all cases caused visual disturbances, paralleled the intensity of the general reaction to the serum. The third report was that of Bedell,[5] who in 1935 described severe and extensive bilateral retinal edema with

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Read before the New York Society for Clinical Ophthalmology, Jan. 2, 1939.

1. Neffson, A. H.: Recurrent Paralysis of the Larynx Following Injection of Tetanus Antitoxin, Arch. Otolaryng. **27**:201-203 (Feb.) 1938.

2. We have not included the case of Walker (Anaphylactic Keratitis, J. A. M. A. **80**:160-161 [Jan. 20] 1923) in which severe keratitis developed two days after the intravenous injection of a "serum" made from the patient's own blood, which caused an immediate anaphylactic reaction.

3. Mason, V. R.: Optic Neuritis in Serum Sickness, J. A. M. A. **78**:88-89 (Jan. 14) 1922.

4. Brown, A. L.: Ocular Manifestations in Serum Sickness, Am. J. Ophth. **8**: 614-618 (Aug.) 1925.

5. Bedell, A. J.: Stereoscopic Fundus Photography, J. A. M. A. **105**:1502-1509 (Nov. 9) 1935.

superficial hemorrhages, which he attributed to serum sickness following the injection of tetanus antitoxin. This cleared up rapidly, leaving few vestiges. Although experimental work indicates the vulnerability of the iris in allergic reactions, apparently no case in which iritis occurred in the course of serum sickness has ever been recorded. Because of this, it was thought worth while to report the following case.

REPORT OF CASE

B. H., a 40 year old salesman, was first seen by one of us (A. C. L.) on March 30, 1938. He had had a productive cough for one week and complained of chills, fever and pain in the chest of twelve hours' duration. The past history was of no importance. No allergic history was elicited. The diagnosis of lobar pneumonia was made despite the absence of signs referable to the chest other than restricted breathing due to pain. The patient was admitted that night to the Beth Israel Hospital, where the diagnosis was confirmed by roentgen examination, which showed involvement of the right middle and lower lobes. The sputum revealed type I of the pneumococcus, and after both intradermal and ocular sensitivity tests to horse serum were found to be negative, Lederle's type I antipneumococcus serum was immediately administered intravenously, 20,000 units at a time, with 1 cc. of epinephrine hydrochloride (1:1,000) subcutaneously. After the third dose of serum, the patient had a moderately severe anaphylactic shock characterized by restlessness, pain in the back, pallor and sweating. After he had recovered from this, a fourth and last dose of serum diluted with 5 per cent dextrose in physiologic solution of sodium chloride by intravenous drip caused no reaction. A total of 80,000 units was given, all on March 31. That night some transient hives were noted.

After the administration of the serum the temperature dropped in two days from a maximum of 105 F. to 101 F., coincidentally with a marked improvement in the patient's general condition. His course was complicated, however, by a pleural effusion, first noted on April 7, which prolonged convalescence considerably, lasting till April 21.

On April 8, nine days after the administration of the serum, there developed serum sickness characterized by an elevation of temperature to 102.4 F., pruritus, urticaria and generalized lymphadenopathy. The spleen was not palpable. The eyes at this time showed no abnormality. The serum sickness lasted two days. After April 10 the temperature was never above 99.4 F., and the patient was discharged from the hospital on April 17. No significant laboratory findings other than those mentioned were noted during his stay in the hospital.

On April 30 serum sickness again developed, manifested this time by an elevation of temperature to 101 F., pains in almost every joint and some transient urticaria. Along with these symptoms the patient suddenly began to note photophobia accompanied by slight pain in each eye and then blurring of vision. There was considerable tearing and some mucopurulent discharge. As all the symptoms continued, he consulted his physician (A. C. L.) on May 3, who prescribed ephedrine sulfate by mouth and drops of epinephrine hydrochloride (1:1,000) for the eyes. The fever and arthritic symptoms abated in a few days, but because there had not been much ocular improvement other than diminution in the discharge, the patient consulted an ophthalmologist (F. H. T.) on May 7.

At the time of ocular examination the presenting symptoms were photophobia and impairment of vision, which, although originally equal in each eye, were now

less marked in the left eye. Little, if any, pain was present. The vision in the right eye was 20/70 and could not be improved with glasses. The vision in the left eye, which was 20/40 + 1, also could not be improved. The preauricular gland on each side was moderately enlarged. The palpebral conjunctiva was injected to a considerable degree in the right eye and slightly in the left eye. A small amount of mucoid discharge was noted. No organisms were found on staining with the Gram stain. The Wright stain showed numerous pus and epithelial cells but no eosinophils or inclusion bodies.

Moderate circumcorneal injection was present in the right eye. On slit lamp examination the corneal epithelium, which did not stain with fluorescein, showed bedewing. Descemet's membrane showed numerous folds. The endothelium on its posterior surface was covered with so much fluffy white material that it appeared as if a piece of cotton wool were covering the entire layer. This deposit precluded further microscopic examination of the interior of the eye, but the anterior chamber was seen to contain much similar cotton-like exudate. The pupil appeared only slightly contracted. The media and fundus could not be examined. The ocular tension was slightly diminished on palpation.

Only slight circumcorneal injection was present in the left eye, but a fibrinous iritis, similar to that in the right eye but less intense, was seen. Much cotton-like exudate was noted both in the anterior chamber and on the endothelium. The pupil was slightly contracted. No abnormalities were found in the lens, vitreous or fundus. The ocular tension appeared normal on palpation.

The most striking thing about the patient was the relative lack of discomfort and lack of reaction in the face of such an extensive process. Because of this, treatment was limited to the instillation of a 1 per cent solution of atropine sulfate three times a day in the right eye and once a day in the left eye in addition to the use of hot compresses every three hours. The improvement was remarkable. The photophobia quickly disappeared; in six days the vision in each eye was 20/20. Within three days a tremendous amount of absorption of the exudate occurred; in the course of a week practically none remained except as small deposits on the endothelium. These, too, disappeared in another ten days. Careful study of the fundi for possible choroidal foci at this time gave negative results.

Studies for focal sources of the iritis, including dental and otolaryngologic examinations, revealed no significant findings. The Wassermann reaction of the blood was negative. A blood smear on May 7 showed no eosinophilia or abnormal proportion of lymphocytes.

COMMENT

Ever since the first experimental investigations into the nature of allergy, the eye has been utilized because of the great advantages it offers for such studies. Horse serum has been used as an antigen in many of these experiments. It was discovered comparatively early by the works of Nicolle and Abt, Sattler, Krusius, Romer and Gebb, Kümmell, von Szily and Arisawa, Zade, Morax [6] and others that allergic ocular inflammatory reactions could be produced by a number of

6. Cited by (*a*) von Szily, A.: Die Anaphylaxie in der Augenheilkunde, Stuttgart, Ferdinand Enke, 1914, chap. 7; (*b*) Woods, A. C.: Ocular Anaphylaxis: I. The Reaction to Perfusion with Specific Antigen, Arch. Ophth. **45**:557-573 (Nov.) 1916.

methods. In all their experiments, however, at some time or other intraocular injection was performed. In 1916 Woods,[6b] using horse serum as one antigen, showed that in dogs sensitized by intraperitoneal injections without injury to the eye a constriction of the pupils occurred when the heads were perfused later with the specific antigen. Small retinal hemorrhages also occurred. In later studies Woods[7] showed that in dogs sensitized by intraocular injections of an emulsion of uveal pigment later injections intraperitoneally caused allergic iridocyclitis in the other eye. Somewhat similar findings had been noted by Dold and Rados.[8] Riehm[9] confirmed this in 1930, using horse serum. All these later experiments were done in studies of sympathetic ophthalmia but are cited here to indicate that the iris responds readily to an allergic inflammation.

In 1930 Iga[10] published a report that is of great interest in connection with the case reported here. His attention had been drawn to focal inflammatory reactions that occurred in the normal eyes of animals in the course of immunization with horse serum. He thereupon began investigations to study the effects on normal eyes of various foreign serums injected parenterally. At no time was the eye itself touched. Iga found that single intravenous injections of even such small amounts of horse serum as 0.5 cc. could produce a diffuse or nodular lymphocytic infiltration of the uvea of both eyes, especially marked in the region of the choriocapillaris. The reaction was proportional to the amount injected; a definite cumulative effect was observed on repeated injections within the preanaphylactic phase, as in immunization. Definite clinical manifestations of uveal inflammation, such as pericorneal injection and clouding of the anterior chamber, with transient plastic iridocyclitis and large choroidal foci could be produced either on two or three injections of 10 cc. of horse serum or on the single injection of at least 20 cc. His work is well illustrated with drawings and photomicrographs. It was Iga's opinion that the single injection given could produce such a reaction because there was a primary toxic effect of foreign serum which, he assumed, acted

7. Woods, A. C.: Ocular Anaphylaxis: V. Experimental Iridocyclitis, Arch. Ophth. **47**:162-172 (March) 1918.

8. Dodd, H., and Rados, A.: Versuche über sympathische spezifische und unspezifische Sensibilisierung, Ztschr. f. Immunitätsforsch. u. exper. Therap. **20**: 273-291 (Dec.) 1916.

9. Riehm, W.: Ueber die Bedeutung der Anaphylaxie für den klinischen Ablauf der sympathischen Ophthalmie, der Tuberkulose und der organgebundenen Infektionskrankheiten (Nach Studium am Auge), Arch. f. Ophth. **123**:361-426, 1930.

10. Iga, F.: Ueber Herdreaktionen an den unberührten Augen nach parenteraler Zufuhr von artfremden Serum, Klin. Monatsbl. f. Augenh. **84**:449-478 (April) 1930.

as a capillary poison. He found that the eye, because of the richly vascular uvea, and the lungs, the liver and the brain and meninges were usually affected.

Thus, the vulnerability of the animal iris to the effects of foreign serum appears to have been adequately proved experimentally. It is surprising in view of this that no clinical cases have been noted until the present time. When one considers the protean manifestations of serum sickness, there seems no reason that it should not occasionally include iritis. In the case here reported all the evidence points to such an etiology. Since the same shock organ, in this case the uvea, is present bilaterally, it follows that both eyes were simultaneously affected; at the same time the other symptoms began. The entire picture suggested a transitory exudative reaction into the anterior chamber, much like that in other synovial cavities, like those of joints. From the beginning it was felt that we were dealing with an unusual sort of process because of the disparity between symptoms and findings. It caused little distress and cleared promptly in the course of a week, so unlike the usual iritis with equally extensive pathologic changes. Even the large amount of exudate disappeared soon. The experimental iritis that Iga produced with horse serum likewise proved mild and transitory. Therefore, while one can never be absolutely certain on clinical grounds as to the etiology of a condition such as iritis, we feel that in this case it was a manifestation of serum sickness.

STREAK RETINOSCOPY

WALTER Z. RUNDLES, M.D.
FLINT, MICH.

Refraction is a procedure of major importance in the practice of ophthalmology. The majority of all patients who consult the ophthalmologist do so because of refractive errors the proper correction of which relieves them of symptoms of ocular distress. It is well known, too, that refractive errors may be etiologically important when symptoms seem to indicate extraocular or intraocular disease. Thus in numerous instances symptoms of apparent muscle imbalance, psychogenic disorder or involvement of the central nervous system can be correctly evaluated only after existing refractive conditions have been thoroughly considered.

The numerous and diverse methods used for refraction may be divided into two general groups: the subjective and the objective. The first involves the use of visual acuity charts, trial lenses etc., and depends on the patient's judgment of his visual capacity with different lens combinations. Objective methods of refraction employ such instruments as the retinoscope and the ophthalmometer and are relatively independent of the patient's visual processes. Although many attempts have been made to emphasize one type of test to the practical exclusion of the other, such is not the present intention. I am in full accord with the prevailing opinion that accurate refraction depends on the skilful use of both types of examination with adaptations appropriate to the individual case. The value of objective methods in routine ocular examination is entirely contingent on the accuracy and reliability of the information obtained. The final criterion by which objective methods are judged remains, of course, the subjective one of visual ability and ocular comfort. Not infrequently, however, subjective tests are found to be of limited utility, as in examining young children or adults of low intelligence, those who are grossly inaccurate in observation or who are unresponsive or antagonistic. Under these circumstances the refractive error is best estimated wholly by objective methods.

The retinoscope provides the most useful and practical means of estimating refractive errors objectively. The outstanding advantage of retinoscopic examination is that the total refractive error of all the dioptric media is measured. Plane mirror retinoscopy as developed

and described by Jackson[1] is virtually the universal method, with the self-luminous type of electric retinoscope the instrument generally preferred.

The purpose of this paper is to discuss another method of retinoscopy, that of streak retinoscopy. Although the streak retinoscope was invented many years ago, its outstanding merits have yet to be generally appreciated. More than a decade ago dissatisfaction with the accuracy and results of plane mirror retinoscopy led me to purchase an electric streak retinoscope.[2] By experimentation a procedure was developed suitable for practical refractive work. Daily use of this instrument for several years since then has provided convincing proof of the unique advantages in accuracy and convenience of this method of estimating refractive errors objectively.

HISTORY OF STREAK RETINOSCOPY

The streak retinoscope was invented in 1900 by Hugo Wolff, of Berlin, Germany. The instrument was designed to give a rectilinear band or streak of light for retinoscopy instead of the round spot of light provided by the plane mirror retinoscope. The optical principles and theory of retinoscopy (skiascopy) and the construction and practical use of his instrument were discussed at length by Wolff in a monograph published in 1903.[3] In later years the subject was further elaborated in a second monograph[4] and in a series of about eleven articles, the most significant of which are listed.[5]

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1. Jackson, E.: Skiascopy, in de Schweinitz, G. E.: Diseases of the Eye, ed. 10, Philadelphia, W. B. Saunders Company, 1924, p. 120.

2. Reid streak retinoscope, J. E. Reid Instrument Co., Philadelphia.

3. Wolff, H.: Ueber die Skiaskopietheorie, skiaskopische Refractionsbestimmung und über mein elektrisches Skiaskopophthalmometer nebst Bemerkung über die Akkomodationslinie und die sphärische Abberation des Auges, Berlin, S. Karger, 1903.

4. Wolff, H.: Skiaskopietheorie vom Standpunkt der geometrischen Optik, der Ophthalmoskopie und entoptischen Wahrnehmung (entoptische Skiaskopietheorie), Berlin, S. Karger, 1905.

5. Wolff, H.: Ueber die Skiaskopietheorie und über mein elektrisches Skiaskopophthalmometer, Wien. med Wchnschr. **54**:2311-2315, 1904; De la théorie skiascopique et de mon skiascopophtalmomètre électrique, Arch. d'opht. **24**:213-219, 1904; Noch einmal meine Skiaskopietheorie, Arch. f. Augenh. **53**:135-148, 1905; Neue Beiträge zur Skiaskopietheorie, Wien. klin. Rundschau **20**:41-44 and 61-64, 1906; Das System der Skiaskopie und Ophthalmoskopie vom Standpunkt der physischen, physiologischen und geometrischen Optik, Ztschr. f. Augenh. **16**: 91-195, 1906; Ueber Schattendrehung und Schattenlauf sowie über das astigmatische Gesichtsfeld in der Skiaskopie, Arch. f. Augenh. **60**:210-254, 1908; Vereinfachte Erörterung über Skiaskopie, nebst einer Uebersicht über 393 Untersuchungen, Ztschr. f. Augenh. **38**:318-359, 1917.

While much of Wolff's work is now only of historical interest, the construction of his instrument, his procedure for retinoscopy and his practical results may be briefly reviewed with profit. In the first streak retinoscope the source of illumination was a small, 12 volt electric bulb with a straight, horizontal rod filament. By means of a convex lens the image of the filament was projected onto a pierced plane mirror. The latter was mounted so that it could be rotated around an axis parallel to the source of light. When the mirror was rotated in this manner, the streak of light, i. e., the image of the straight filament, was turned through 180 degrees. In this way the eye was examined with the streak of light passing through any desired meridian.

The procedure which Wolff developed for objective refraction resembles in many ways that used today. Thus he emphasized the basic principle of the streak retinoscope, namely, that with this instrument the refraction is always to be determined in one meridian of the eye at a time—in the meridian lying at right angles to the streak. The "with" and "against" movements of the fundus reflex and the point of reversal were observed and interpreted as they are today. Both the stable method of retinoscopy at a fixed distance and the labile method with variable distance were used to measure the strength of correcting lenses. The axis of astigmatism was found in substantially the same manner as is subsequently described.

From the standpoint of practical utility, Wolff believed that his method transformed retinoscopy from a previously gross control method into one of the most exact ophthalmometric measuring methods. He insisted from his earliest work (1903) that the refraction of the eye, including the astigmatic correction, could by his method be estimated objectively to within 0.25 diopter, or even 0.1 diopter if one wished, and that the axis of the cylinder could be determined to an accuracy of 1 degree. The objective and subjective refractive estimations for 92 astigmatic eyes were tabulated for comparison to show that this accuracy was obtained in 80 per cent of the total cases. In the 20 per cent minority a greater accuracy was obtained than was possible with any other method. In Wolff's last paper (1917) the same conclusions were reaffirmed after seventeen years of experience with the method. The data on 393 cases were then tabulated to illustrate the accuracy of his procedure under various circumstances.

Although streak retinoscopy became well known throughout Germany due to Wolff's work, it did not attract a wide scientific following, perhaps because of the prevailing attitude regarding the medical importance of refraction itself. In other countries the method attracted even

less attention. In 1917 the distinguished British ophthalmologist R. H. Elliot commented as follows:[6]

> It is a good many years since Hugo Wolff brought out his electric retinoscope with a single line of light, and developed its technique in a monograph of truly Teutonic thoroughness, and yet his instrument is still almost unknown in Great Britian. I have used it now certainly for more than a decade, and I should indeed feel lost without it, so much so that I have tried to get an English instrument made on similar lines. . . . To my mind the advantages of the instrument cry aloud for recognition.

The principle of the streak retinoscope was later discovered independently in this country by J. C. Copeland.[7] While he was using a plane mirror retinoscope the frosted glass used to diffuse the image of the filament was accidentally broken. This caused the filament line to be projected instead of the conventional spot of light produced by the diffusing disk which covered a small aperture over the lamp. The filament image was S shaped, and the middle portion when projected over the pupil of the eye produced a straight line reflex. Further experimentation showed the value of the straight line reflex in retinoscopic work, and accordingly a retinoscope was designed to give this type of illumination. The instrument developed was patented in 1927 and accepted by the Council on Physical Therapy of the American Medical Association in 1935.[8] The illumination originates from a small bulb the filament of which is bent to provide a linear source of light. The bulb can be rotated 180 degrees as well as moved to and from a condensing lens to vary the angularity of the light leaving the mirror. At one extreme the rays converge to cross about 9 inches (22.8 cm.) in front of the instrument. At the other extreme the rays diverge, giving a "plano mirror effect." The use of this instrument was briefly described recently by Maxwell.[9]

It is interesting finally to note the type of plane mirror retinoscope (skiascope) used by Clapp[10] in his extensive investigation concerning the accuracy of retinoscopy in objective refraction. The enviable results recorded were obtained by using an instrument the bulb of which had a long horizontal filament which created an artificial band in the illuminating spot of light. It was necessary to find the point of reversal in both the lesser and the greater curvatures, "the reflection

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6. Elliot, R. H.: Errors of Refraction, Brit. J. Ophth. **2**:313-322, 1918; cited by Copeland.[7]

7. Copeland, J. C.: Personal communication to the author.

8. Copeland Refractoscope Acceptable, report of the Council on Physical Therapy, J. A. M. A. **105**:1982-1983 (Dec. 14) 1935.

9. Maxwell, J. T.: Outline of Ocular Refraction, Omaha, Medical Publishing Company, 1937.

10. Clapp, C. A.: Accuracy of Skiascopy as Based upon a Study of Fifteen Thousand Eyes, Am. J. Ophth. **7**:523-526, 1924.

of the filament being a right angle to the curvature to be determined." I regard this as an additional verification of the principle of the streak retinoscope.

STREAK RETINOSCOPY

The theory underlying streak retinoscopy, as was originally pointed out by Wolff, is precisely the same as that underlying all other types of retinoscopy. The general principles of retinoscopy need not be reviewed here, since excellent accounts are available in the books by Thorington,[11] Duke-Elder,[12] de Schweinitz,[13] Berens[14] and Maxwell.[9] A complete description is given by Pascal.[15]

Two optical systems are involved in retinoscopy, the first of which is the illumination system by which light is directed into the eye to illuminate a portion of the retina. The retina then acts as a secondary source of light for the second optical system, the observation system. The observer is concerned with the fundus reflex, an image of the retinal illumination which appears to lie in the plane of the pupil. The form and behavior of the fundus reflex depend on the type of retinal illumination provided by the retinoscope employed and on the optical construction of the eye as a whole. With the streak retinoscope the fundus reflex appears as a clear, bright band or ribbon of light in the pupil more or less parallel to the streak of light from the instrument. The reflex is brighter and the boundary between light and shadow sharper and more clearcut than with other retinoscopes because the source of illumination lies close to the mirror and because of the focusing lens system employed. The reflex is band shaped because the illuminating streak of light, being narrower than the aperture of the pupil, illuminates a narrow, rectangular area of the retina. Since the fundus reflex is an image of the retinal illumination, it likewise is band shaped. Contrary to the fundus reflex seen with the plane mirror retinoscope, this band-shaped fundus reflex has no relation to the presence or absence of astigmatism. The reflex disappears, and the pupil is filled with light when the mirror of the retinoscope lies at the point of reversal or far point of the lens system of the eye with accommodation at rest.

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11. Thorington, J.: Refraction of the Human Eye, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1930.

12. Duke-Elder, W. S.: The Practice of Refraction, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1935.

13. de Schweinitz, G. E.: Diseases of the Eye, ed. 10, Philadelphia, W. B. Saunders Company, 1924.

14. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936.

15. Pascal, J. I.: Modern Retinoscopy, Including the Principles and Practice of Velonoskiascopy, London, Hatton Press, Ltd., 1930.

Movements of the fundus reflex are observed and interpreted with streak retinoscopy in the ordinary manner, except the light band itself is watched rather than the bordering shadow. With modern streak retinoscopes the angularity of the emergent light and the width of the streak can be varied, or the light rays can be crossed in front of the instrument (concave mirror effect). This adjustment is prone to cause confusion. For simplicity of use, I adjust the streak, light uncrossed, to a width of 4 to 6 mm. at a working distance of 1 meter. No further adjustments are made. With this plano mirror system a "with" movement of the fundus reflex denotes hypermetropia, emmetropia or myopia less than the strength of the lens equivalent to the working distance. An "against" movement denotes myopia of an amount greater

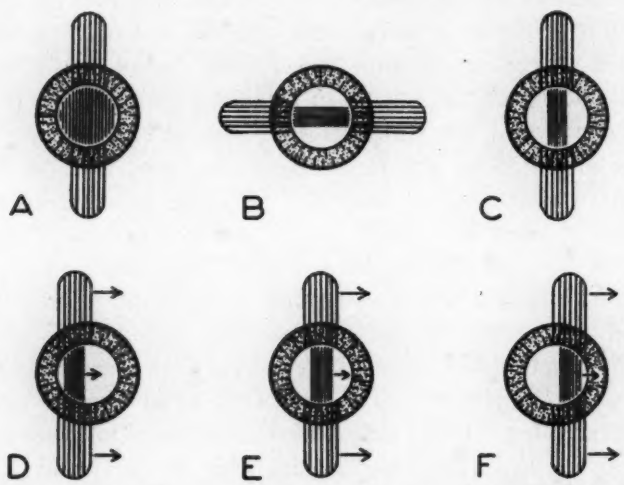

Fig. 1.—*A*, neutral reflex. The pupil of the eye is entirely filled with light. *B* and *C*, the band-shaped fundus reflex in the pupil parallel to the retinoscopic streak. *D*, *E* and *F*, diagrams showing "with" movement, both reflex and streak moving in the same direction.

than the lens equivalent to the working distance. It need only be remembered that light crossing in front of the observer, as in the higher grades of myopia, gives an "against" movement; light emerging from the eye which does not cross in front of the observer gives a "with" movement.

The speed of movement of the fundus reflex also provides useful information concerning the refraction of the eye. The higher the refractive error, either myopic or hyperopic, the slower is the movement of the reflex. At the point of reversal or neutralization of the reflex, when the pupil is either completely dark or completely filled with light, the speed of movement may be considered infinite.

A most important advantage of streak retinoscopy lies in the accuracy with which the axis of astigmatism can be determined. When an astigmatic eye is examined with the streak retinoscope, the fundus reflex exhibits a number of phenomena closely related to those observed by Lindner [16] with the cylinder retinoscope. In a hypothetic case in which at a given working distance the reflex in one meridian has been neutralized, if the streak of light is turned 90 degrees and then passes exactly through the axis of astigmatism, a bright, sharply defined reflex band is seen. When the movement of the reflex is tested, both the reflex and the light streak are seen to move in directions exactly parallel, either with or against. If the streak is rotated a few degrees away from the axis of astigmatism, the reflex becomes much more poorly defined and

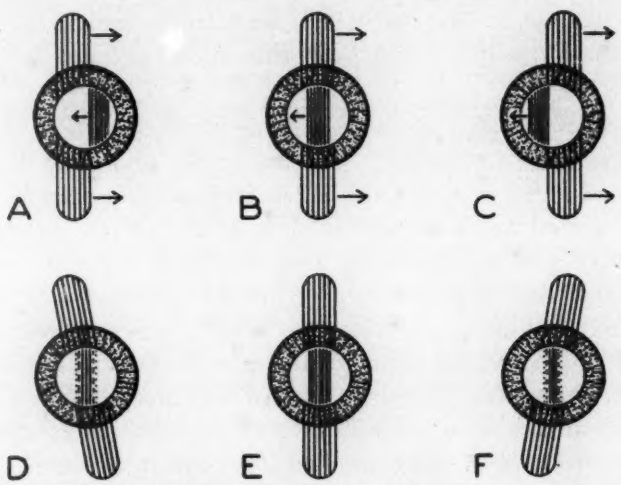

Fig. 2.—*A*, *B* and *C*, diagrams showing "against" movement, streak and reflex moving in opposite directions. *D*, *E* and *F*, diagrams of a 90 degree axis of astigmatism. A bright, clearly defined reflex is seen when the streak passes exactly through the axis of astigmatism as in *E*. Rotation of the streak, *D* and *F*, decreases the clarity of the reflex, but it remains in the astigmatic meridian.

tends to remain fixed in the astigmatic meridian, producing a break in the alinement between the streak of light on the face and the reflex in the pupil. A peculiarity in the movement of the reflex is now noted also. It moves in a direction oblique and rather eccentric to that of the streak, tending to assume a position intermediate between that of the real axis of astigmatism and the streak of light on the face. The exact axis of very low astigmatic errors is easily found by rotating the streak until both streak and reflex move in parallel directions.

16. Lindner, K.: Die Bestimmung des Astigmatismus durch Schattenprobe mit Cylindergläsern, Berlin, S. Karger, 1927.

The magnitude of the astigmatic error can be measured readily by neutralizing with cylinders the reflex in the astigmatic meridian. With the use of cylinders an additional check can be made on the axis of astigmatism. If the cylinder is improperly placed, the following phenomena (Lindner) appear: (1) mixed astigmia, "with" movement in one meridian and "against" movement in the other; (2) oblique astigmia, with the astigmatic reflex oblique to the axis of the cylinder in place, and (3) mobile astigmia, in which the principal optical meridians have apparently shifted.

With the foregoing principles in mind, a procedure suitable for routine ocular refraction with the streak retinoscope is readily designed. When one becomes experienced and expert in the method, subtle differences in the appearance of the reflex enable one to make almost automatic judgments and arrive at accurate retinoscopic estimations with exceeding rapidity. The procedure to be outlined is that which I use:

The patient is seated in the examining chair, the room is darkened, and the phoropter is adjusted. The use of the phoropter here as with other types of retinoscopy is most convenient and saves much time. The patient is directed to focus on a small light 20 feet (6 meters) distant, or with cycloplegia the patient may look into the retinoscopic mirror or at the illuminated disk adjacent to it. The observer sits at a distance of either 66 cm. (26 inches) or 1 meter (40 inches) in a position as close as possible to the visual axis of the eye to be examined. A lens representing the working distance may or may not be placed before the patient's eye at this time, according to the operator's preference. The reflex is somewhat more easily studied if no lens intervenes.

As soon as the streak is thrown on the pupil, a white band of light parallel to the axis of the streak is seen. By an adjustment on the handle of the instrument the streak is rotated about the pupil and the characteristics of the fundus reflex studied. Is the band wide or narrow? Does it move quickly or slowly? Is it clearcut or indistinct? Has it the same characteristics in all meridians? The expert is able to infer much from this initial inspection. As a rule, a narrow band denotes hyperopia or hyperopic astigmatism; a wide band, myopia or myopic astigmatism. When the band is equal in all meridians there is no astigmatism. A "with" movement of the reflex means that the far point of the eye lies beyond the observer; an "against" movement, that it lies between the observer and the patient.

The reflexes are now neutralized systematically. If a "with" movement is observed in all meridians, plus spheres are added until a neutral reflex is obtained, usually first in the meridian in which the reflex is less distinct. If a sphere neutralizes the reflex in all meridians, there is no astigmatism. If a band-shaped reflex having a "with" movement

remains in one meridian, astigmatism is present, and the axis should now be carefully determined as previously outlined. The reflex in the astigmatic meridian is next neutralized with plus cylinders. Finally, the value of both cylindric and spherical corrections is checked by shortening the working distance a few centimeters, whereupon all meridians should show a "with" movement of the reflex, becoming neutral again when the original working distance is resumed. The final retinoscopic measurement is found by adding algebraically to the lenses in place a minus sphere representing the working distance. For 66 cm., a minus 1.5 diopter sphere is added; for 1 meter, a 1 diopter sphere is added. It is seen that this procedure is applicable to all cases of hyperopia and of simple and compound hyperopic astigmatism.

If on initial inspection an "against" movement of the reflex appeared in all meridians, minus spheres are added to neutralize the reflex. If astigmatism is present, a spherical lens will not neutralize all meridians. In this case the strongest meridian is neutralized with minus spheres, giving a neutral reflex in one meridian and a "with" movement in the meridian at right angles to it. The axis of astigmatism is now determined, the astigmatic reflex neutralized with plus cylinders and the value of both lenses checked by the approach-receding method as before. A final correction is made for the working distance. In the neutralization of "against" movements, since "against" movements are harder to see than "with" movements, the error at first may be overcorrected with minus lenses to produce a "with" movement, following which the strength of the lens is decreased until the reflex is neutralized. The foregoing procedure can be used in cases of myopia and of simple and compound myopic astigmatism.

In mixed astigmatism, showing "with" movement in one meridian and "against" movement in the other, the "against" movement is first neutralized with minus spheres, then the "with" movement is neutralized with plus cylinders.

The subjective test may then be started with the correction for the working distance, as determined retinoscopically, in place.

When one is beginning to use the streak retinoscope it is best to study the reflex in dilated pupils. After experience has been gained, a dilated pupil is no longer necessary, and, indeed, it is often an advantage to do retinoscopic examination on normally contracted pupils, for then only the reflex in the visual zone of the pupil is seen. Another advantage peculiar to the streak retinoscope is that the reflex is narrow enough and sufficiently well defined that retinoscopic examination can be carried out routinely without the use of mydriatic drugs not otherwise indicated.

COMMENT

Accuracy in refraction and how to achieve it is a subject that has been discussed many times both before and since the appearance nearly thirty years ago of Edward Jackson's well known article on the subject.[17] It is now generally accepted that refractive errors may be responsible for widespread symptoms throughout the body and that ametropia even of low or moderate degree should be fully corrected. It is further realized that every inaccuracy in the estimation of ametropia will lessen the chance of relieving the patient. In spite of the confusing array of instruments and methods at present available for measuring refractive errors, much of the refraction done today should probably be classified as "inexpert." Many ophthalmologists have, as medical students or even later, undergone refraction repeatedly before obtaining the relief so easily possible with proper correction. More pertinent evidence in this regard is provided by the large number of patients consulting the ophthalmologist who are already wearing glasses which were or have become grossly inaccurate. If the practical results of refraction are to be improved, it is of the highest importance that methods and procedures most likely to be successful in the hands of those who use them should be developed and emphasized in writing and in instruction.

Accurate refraction requires a careful objective as well as subjective examination. In my opinion there is a widespread tendency to overemphasize numerous refinements of subjective testing while minimizing the value of objective results, with slight appreciation of the intimate, dependent relation that exists between the two. The subjective test is markedly facilitated if one is able, from the retinoscopic findings, to begin the test with approximately the required sphere and cylinder in place, the axis of the latter being properly placed. Under these circumstances one has all the advantages of solving a problem in algebra, knowing the answer in advance. The subjective test then does not last so long as to exhaust the interest and endurance of the patient when the results of the most delicate subjective tests become progressively less accurate and more confusing.

There is, of course, no doubt that ordinary plane mirror retinoscopy has produced results eminently satisfactory in the hands of some operators. The criticism and doubts of others, however, show that success has not been universal. I believe that streak retinoscopy is inherently an easier and more accurate method of retinoscopy, producing results more clearcut and easier to interpret. The method is scientifically grounded, simple in practical application and deserving of a wider trial than has yet been afforded.

17. Jackson, E.: Accuracy in the Measurement of Refraction, Ann. Ophth. 18:703-712, 1909.

SUMMARY

The development and use of the streak retinoscope from its invention in 1900 by Hugo Wolff is reviewed. The use of the streak retinoscope is compared with that of the ordinary plane mirror retinoscope, and a procedure suitable for routine streak retinoscopy is outlined. Among the advantages of the method are: the clarity of the fundus reflex, the ability to measure accurately the refraction in different meridians of the eye individually, the accuracy with which the axis of astigmatism can be determined and the ability to perform retinoscopic examination routinely with contracted pupils.

HODGKIN'S DISEASE OF THE LID

REPORT OF A CASE

DANIEL KRAVITZ, M.D.

BROOKLYN

Involvement of any part of the eye with Hodgkin's disease is sufficiently rare to warrant reporting. It becomes increasingly interesting when it occurs in a person of an age far beyond that at which the disease is suspected and rare indeed when the diagnosis is established through the intermediary of the ophthalmologist.

REPORT OF CASE

C. S., a woman aged 82, was seen on Dec. 12, 1937, for refraction. There was sclerosis of both lenses, and the best vision obtained after correction was 20/70 in the right eye and 20/100 in the left. A small cystic tumor was palpated at the left superior orbital border near the inner angle.

On April 20, 1938, the patient returned because of ptosis of the left upper lid. The tumor had increased greatly in size, and as it was felt that it was interfering with elevation of the lid, removal was advised.

On April 25, at the Brooklyn Eye and Ear Hospital, a tumor a little over 1 inch (2.5 cm.) long was removed. It was firm in consistency and was enveloped in a thick white capsule. The tumor was dissected from the underlying periosteum without any difficulty except at its inner end, where it merged with the underlying structures and could not be dissected but had to be cut away. It was felt that the growth was a fibroma.

After operation the lid could be elevated to a considerable extent. In a few weeks the remaining tumor tissue had increased in size, the ptosis had returned, and two similar tumors had appeared along the upper border of the left orbit.

To my great surprise, on June 1 I received a communication from Dr. DeVeer, the pathologist at the hospital, stating that the tumor had all the histologic features of Hodgkin's disease. Reexamination at this time failed to reveal any enlargement of the superficial lymph glands of the neck or face. A roentgenogram of the chest on June 30 did not show any masses or enlarged mediastinal lymph nodes. The blood count was normal except that it showed a mild anemia. Roentgen therapy was advised.

The members of the family remembered that a few years past the patient had been treated with roentgen irradiation for enlargement of the glands on the sides of the face at the Brooklyn Cancer Hospital. Inquiry elicited the following history from this hospital:

"The patient came to the hospital for swelling on each side of the face. A diagnosis of bilateral parotitis was made, and she was treated with roentgen irradiation once weekly from March 21 to May 11, 1934, after which the swelling

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Read before the American College of Surgeons at the Brooklyn Eye and Ear Hospital, Oct. 19, 1938.

disappeared. She returned in October 1934, because of a cystlike swelling of the right lower lid. Some small shotty lymph nodes of the superficial cervical glands on the right side were observed. The patient was referred to the ophthalmic clinic and disappeared from observation. No biopsy was made."

The patient left my care and went to the Memorial Hospital, New York, for treatment. The following report was received from this hospital:

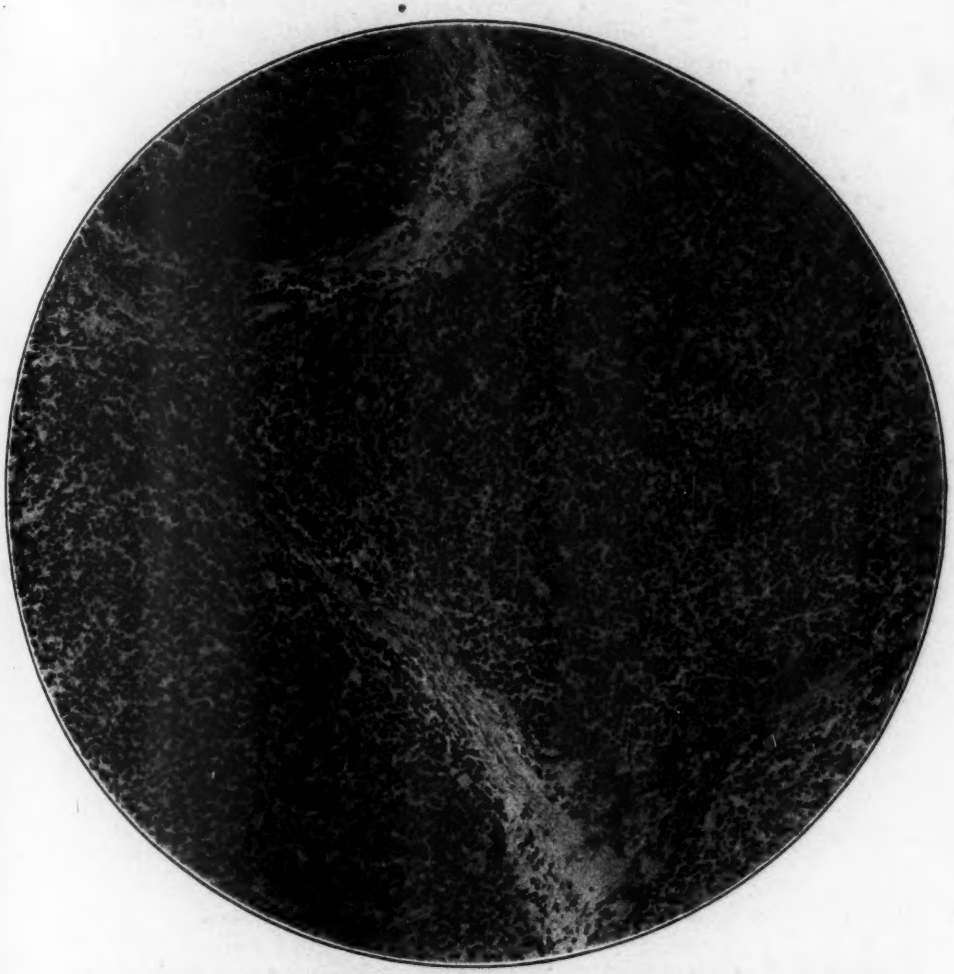

Fig. 1.—The tumor tissue under low magnification, showing considerable pleomorphism. Giant cells and hyperchromatic nuclear masses are numerous in this field. There is also some fibrosis.

"The diagnosis on histologic examination of some aspirated material was dense uniform lymphoid tissue consistent with Mickulicz' disease. The diagnosis based on examination of some material from the tumor sent from the Brooklyn Eye and Ear Hospital was malignant tumor, classified as giant cell reticulum cell lymphosarcoma."

Under roentgen therapy the swelling of the glands on each side of the face disappeared, only to return more markedly in a few weeks. Further roentgen

therapy again caused the swelling to disappear. Two months prior to the writing of this report, signs of pressure in the chest began to develop. A roentgenogram of the chest showed large masses of glands. However, because of the patient's poor physical condition, roentgen therapy of the chest was not deemed advisable. She is still under treatment at the Memorial Hospital.

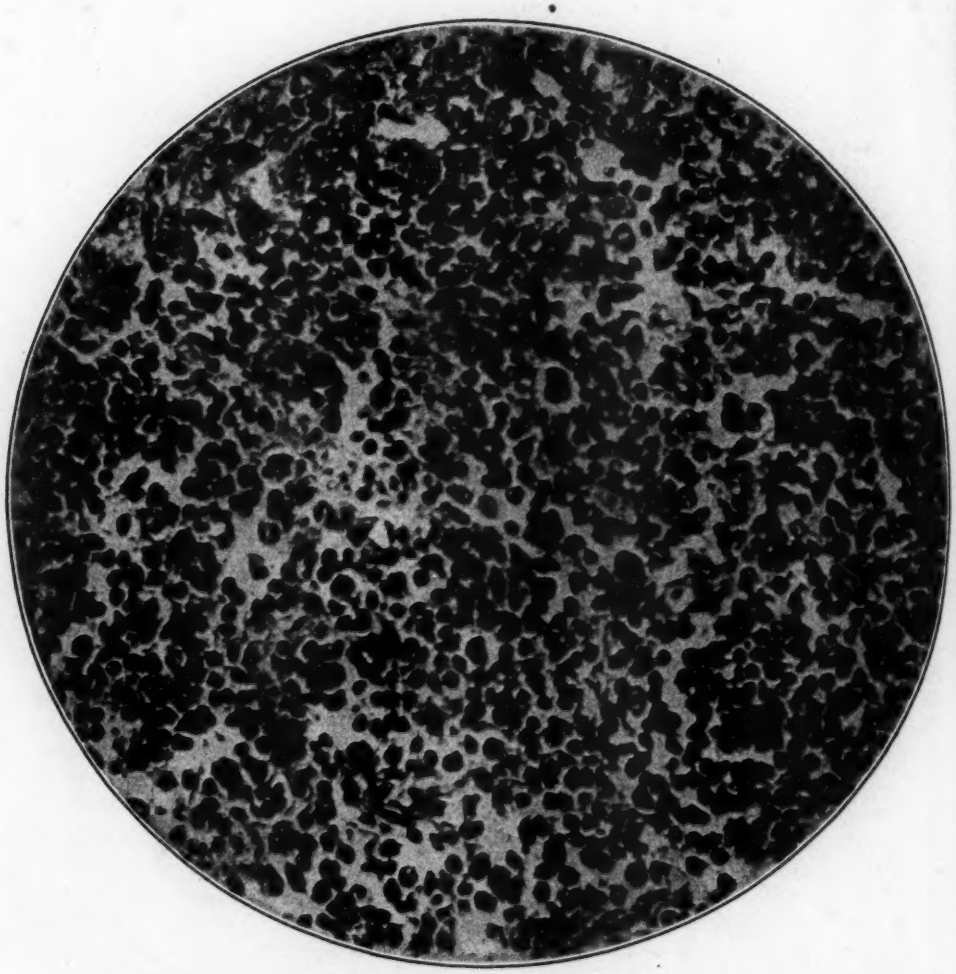

Fig. 2.—A section under higher magnification, showing giant cells of the Reed type, numerous reticulum cells and many leukocytes.

COMMENT

The differences in the diagnosis of different pathologists from histologic examinations of material from the same patient only emphasize the difficulties in classifying this most interesting disease entity.

In 1832, under the title of "Some Morbid Appearances of the Absorbent Glands and Spleen," Hodgkin [1] described 7 cases of a new disease entity. The condition in only 2 of these cases has subsequently been found to fit the description of the disease which now bears his name. The condition in some of the cases was tuberculosis and in the others, leukemia.

Classification of the disease is difficult. Horder [2] stated that he was not certain whether to classify it as a neoblastoma or as an inflammation. The disease shares the features of each condition. Its main expression is tumor formation, but the existence of fever, the occurrence of natural remissions and the histologic characteristics of the many lesions are identical with the course the same tissue takes when subjected to microbic infection. Boyd [3] also expressed the belief that in spite of the fatal outcome the pleomorphism shown by the histologic picture is one usually associated with a chronic inflammatory lesion rather than with a malignant process. According to him, this disease may occupy an important borderline position between inflammation and neoplasia. The disease is frequently preceded by a sore throat, and in the majority of cases the cervical glands are first involved. This occurrence caused Horder [2] to express the opinion that the infective agent enters in the vicinity of the cervical glands. He also stated that an infection of known nature, such as a tuberculous or a pyogenic infection, may precede the pathologic agent at its point of entrance.

The exact causation of the disease is not known. Probably the most persistent and insistent view has been that it is some form of tuberculosis. Sternberg [4] maintained that it is due to the toxin of tuberculosis. Ewing [5] demonstrated that tuberculosis does not develop in guinea pigs inoculated with material from patients with lymphadenoma until from nine months to a year afterward. Gordon [6] was unable to cultivate the

1. Hodgkin, T.: Some Morbid Appearances of the Absorbent Glands and Spleen, Med.-Chir. Tr. **17**:68, 1832.

2. Horder, T.: A Clinical Concept of Lymphadenoma or Hodgkin's Disease, in Horder, T., and others: Rose Research on Lymphadenoma, Bristol, England, John Wright & Sons, Ltd., 1932.

3. Boyd, W.: Text Book of Pathology, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 319.

4. Sternberg, C.: Ueber eine eigenartige unter dem Bilde der Pseudoleukämie verlaufende Tuberkulose des lymphatischen Apparates, Ztschr. f. Heilk. **19**:21, 1898.

5. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 407.

6. Gordon, M. H.: Studies of the Etiology of Lymphadenoma, in Horder, T., and others: Rose Research on Lymphadenoma, Bristol, England, John Wright & Sons, Ltd., 1932.

tubercle bacillus from material from patients with typical Hodgkin's disease. He expressed the belief that too much attention has been paid to tuberculosis as a cause, particularly since it has been shown that lesions resembling tuberculosis microscopically and macroscopically may be produced by certain fungi, yeasts and molds.[7] Gordon also failed to substantiate the claim that Hodgkin's disease is a form of mycosis.[8] Fränkel and Much[9] found gram-positive, nonacid-fast bacillary and granular bodies which they thought might be the cause of Hodgkin's disease. This finding was confirmed by Kusunoki.[10] A diphtheroid bacillus was found by Bunting and Yates.[11] The latter were able to produce granular swellings which histologically resembled the granuloma of Hodgkin's disease. Rosenow confirmed their claims, and he and Billings[12] treated a number of patients with a vaccine prepared from this organism, with favorable results. Pröscher and White[13] claimed that the disease is due to a spirochete. However, none of the foregoing claims were substantiated by the research work of Gordon, who expressed the belief that the most recent evidence in favor of a filtrable virus as its cause is the most promising.

Gordon[14] injected some emulsified gland from patients with Hodgkin's disease into the brains of rabbits and guinea pigs. Symptoms of marked involvement of the brain and spinal cord, such as those of paraplegia, appeared. Postmorten examination showed signs of severe inflammation of the nerve tissues. Lymphocytic infiltrations were not visible. Allen and Mercer[15] reported 2 cases in which clinical and

7. (*a*) Schenck, B. R.: On Refractory Subcutaneous Abscess Caused by a Fungus Possibly Related to the Sporotricha, Bull. Johns Hopkins Hosp. **9**:286, 1898. (*b*) Stollard, J. L., and Cutler, E. C.: Torula Infection in Man, Monograph 6, Rockefeller Institute for Medical Research, 1916.

8. Dias, E. C.: Adenomycosis, New Orleans M. & S. J. **70**:598, 1918.

9. Fränkel, E., and Much, H.: (*a*) Bemerkungen zur Aetiologie der Hodgkinschen Krankheit und der Leukämia lymphatica, München. med. Wchnschr. **67**: 685, 1910; (*b*) Weitere Untersuchungen über Lymphogranulomatose, Ztschr. f Hyg. u. Infektionskr. **9**:39, 1923.

10. Kusunoki, M.: Zur Aetiologie der Lymphomatosis granulomatosa, Virchows Arch. f. path. Anat. **214**:184, 1914.

11. Bunting, C. H., and Yates, J. L.: Cultural Results in Hodgkin's Disease, Arch. Int. Med. **12**:236 (Aug.) 1913.

12. Billings, F., and Rosenow, E. C.: The Etiology and Vaccine Treatment of Hodgkin's Disease, J. A. M. A. **61**:2122 (Dec. 13) 1913.

13. Pröscher, F., and White, W. C.: Ueber das Vorkommen von Spirochetes bei pseudoleukämischer Lymphdrüsenhyperplasie, München. med. Wchnschr. **54**: 1868, 1907.

14. Gordon, M. H.: Recent Advances in the Pathology and Treatment of Lymphadenoma, Proc. Roy. Soc. Med. **27**:1035, 1934.

15. Allen, I. M., and Mercer, J. O.: Spinal Symptoms with Lymphadenoma, J. Neurol. & Psychopath. **17**:1, 1936.

autopsy observations matched the foregoing experimental findings. The spinal fluid in each case gave evidence of an inflammatory reaction. These authors agreed with Gordon that this is evidence in favor of a filtrable virus as the cause of the disease.

McJunkin [16] called attention to the resemblance of certain cytologic changes produced by the Rous virus in experimental fowl sarcoma to those present in lymphadenoma. Coley [17] maintained that the clinical features of Hodgkin's disease so closely resemble those of sarcoma that it is often impossible to differentiate the two conditions, and even the pathologists are divided in their opinion when looking at a specimen. Coley expressed the belief that this fact furnishes additional evidence in favor of the infectious origin of sarcoma. Ewing [5] has shown that Hodgkin's disease may become sarcomatous—Hodgkin's sarcoma. However, he stated that the sarcoma is the result of chronic irritation on the neighboring endothelial cells or that as a result of vigorous proliferation of the lymphoid cells these cells become sarcomatous. Turnbull,[18] however, called the disease a lymphosarcomatoid condition and regarded it as an inflammatory reaction.

As previously stated, the cervical glands are the most frequently affected; this is thought to be the result of a previous local irritation in the mouth and tonsils. The glands are hard and discrete, and the glandular swelling then spreads to the other parts of the body. Later the glands may fuse, as in tuberculosis. Rarely the parotid glands may be first involved, and the disease may resemble Mikulicz' disease. Symers [19] and Ewing,[19a] however, stated that the superficial glands are not first involved but that they are the outward manifestation of an internal disorder. According to them, the thoracic and abdominal glands are first involved. Osler [20] called attention to a rare type of disorder called lymphoid ossium in which there are multiple tumors of the bone marrow and the periosteum. He was doubtful about considering this condition Hodgkin's disease. However, in Allen and Mercer's [15] cases, definite osseous and periosteal invasions were found.

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16. McJunkin, F. A.: Histologic Resemblance of Rous Chicken Sarcoma No. 1 to Hodgkin's Granuloma, J. Cancer Research **12**:47, 1928.

17. Coley, W. B.: (*a*) Further Evidence in Support of the Theory That Hodgkin's Disease Is a Type of Sarcoma, Tr. Am. S. A. **26**:560, 1908; (*b*) A Report of Recent Cases of Inoperable Sarcoma Successfully Treated with Mixed Toxins of Erysipelas and Bacillus Prodigiosus, Surg., Gynec. & Obst. **13**:174, 1911.

18. Turnbull, H. M., cited by Rolleston, H.: Lymphadenoma (Hodgkin's Lymphogranuloma), Lancet **2**:1209, 1925.

19. Symers, D.: Clinical Significance of Pathological Changes in Hodgkin's Disease, Am. J. M. Sc. **167**:157, 1924.

19a. Ewing, cited by Rolleston,[26] p. 1210.

20. Osler, W.: The Principles and Practice of Medicine, ed. 8, New York, D. Appleton and Company, 1912, p. 749.

Histologically, the disease is characterized by marked variation in the picture and a pleomorphism. One sees mainly large pale cells of an "epithelioid" type, so that there is a resemblance to the hyperplastic form of tuberculosis. These cells are derived from the reticuloendothelial cells. More characteristic is the presence of large reticulum cells, giant cells, which are seen in the process of division. Many are multinuclear, and some are mononuclear; when they are single, they are often convoluted or ring shaped. The nuclei are large and stain darkly against a faintly staining cytoplasm. These are the Sternberg, or Dorothy Reed, cells. The presence of these cells is essential to the diagnosis of lymphadenosis. Eosinophilic leukocytes in great profusion complete a characteristic picture. These may be absent. However, all pathologists agree that when they are present a diagnosis of Hodgkin's disease is favored.

Lymphocytes, plasma cells and polymorphonuclear cells may all be present to complicate the picture. The last are usually secondary to necrosis. An increase in the fibrous tissue is another change, in the absence of which no lesion is considered quite typical. This fibrosis increases with time and may become dense. At times the microscopic picture may be more neoplastic in appearance, with many mitotic figures and a tendency to invasion of the surrounding tissue. This is the picture presented by the Hodgkin's sarcoma of Ewing.

Hodgkin's disease is the result of an irritation of the reticuloendothelial tissue. It is interesting to note that the study of the reticuloendothelial system originated with the eye. In 1863 von Recklinghausen [21] described ameboid cells in an inflamed cornea and in the omentum of different animals. These cells could be distinguished from pus corpuscles. He expressed the belief that they came from the fixed connective tissue cells. Further study and elaboration of this complex system were carried on by the process of vital staining.

Maximow [22] objected to the inclusion of the term endothelial in the picture. According to him, the reticulum is not composed of well defined units but of a series of spongelike syncytia of nuclei and protoplasm. This reticulum has multipotentialities which are retained in adult life, just like the mesoderm from which it is derived. The reticulum is distributed as a ground substance in the lymphoid and myeloid tissue and in the red pulp in the spleen. In the lymphatic glands it lines the lymph sinuses. Under the proper stimuli, individual cells separate and give origin to lymphocytes, histiocytes, free macrophages and fiber-bear-

21. von Recklinghausen, F.: Ueber Eiter und Bindegewebskörperchen, Virchows Arch. f. path. Anat. **28**:157, 1863.

22. Maximow, A., in von Möllendorff, W.: Handbuch der mikroskopischen Anatomie des Menschen, Berlin, Julius Springer, 1927, vol. 11, pt. 1.

ing cells of various kinds. Lang [23] has furthermore proved the possibility of direct myeloid transformation. Maximow stated that reticulum is derived from the mesoderm and not from the endothelium of the vascular and lymph channels; therefore reticuloendothelium is a misnomer, because it links two different types of cells. Medlar [24] considered the Dorothy Reed cells to be megakaryocytes derived from the bone marrow.

The differential diagnosis is still beset with many difficulties, and, as Watson [25] stated, a differentiation between Hodgkin's lymphosarcoma and leukemia may be impossible from the study of one node.

The close association between Hodgkin's disease and tuberculosis has been noted from the beginning. The giant cells in the two conditions are distinct. The glands in Hodgkin's disease have a tendency to remain discrete, and the steady, progressive and fatal termination is different from the clinical course of tuberculosis. Rolleston [26] explained the close association of the two conditions on the basis that Hodgkin's disease either activates a tuberculous process or else makes the glands more predisposed to a tuberculous infection.

Hodgkin's disease is differentiated from leukemia by the almost normal blood count, whereas in leukemia there is a high lymphocyte count. The differentiation from the aleukemic form of leukemia is more difficult, but histologic sections do not show the giant cells and the eosinophils of Hodgkin's disease.

The greatest difficulty lies in differentiating Hodgkin's disease from lymphosarcoma, which may resemble it clinically. In lymphosarcoma the glands form larger masses. This condition is more frequent in the fourth decade of life, while Hodgkin's disease occurs more frequently in the second and third decades. The consistency of the tumor in lymphosarcoma is not as hard as that in Hodgkin's disease. Histologically, the predominant cell is the lymphocyte. The presence of eosinophils and the absence of a tendency to invasion and infiltration of the surrounding tissue point to Hodgkin's disease. While all the authors stated that the two diseases are distinct entities, they expressed the opinion that all diseases of the blood may have a common etiology. Different glands in the same patient may show the characteristics of each of the diseases. Particularly difficult to diagnose are the early stages

23. Lang, F. J.: Experimentelle Untersuchungen über die Histogenese der extramedullären Myelopoese, Ztschr. f. mikr.-anat. Forsch. **4**:417, 1926; Myeloid Metaplasia, Folia haemat. **43**:95, 1930.

24. Boyd,[3] p. 831.

25. Watson, C. J., in Downey, H.: A Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, vol. 4, p. 3074.

26. Rolleston, H.: Lymphadenoma (Hodgkin's Lymphogranuloma), Lancet **2**:1209, 1925.

when transitional forms are present. This caused Watson [25] to state that there may be a fundamental relation between all diseases of the blood.

The course of Hodgkin's disease is progressive; the anemia increases, and there are episodes of fever, which may last for days, the Pel-Ebstein type of fever. The glands enlarge, so that there may be pressure symptoms in the chest or abdomen. The skin becomes bronzed, as in Addison's disease. Itching is a marked and fairly constant symptom. Gradually the patient dies of inanition or most probably from an intercurrent infection.

Treatment is palliative and prolongs the remissions. Arsenical preparations have proved of definite benefit. The best treatment is roentgen irradiation of the enlarged glands. It is remarkable to see the swelling disappear. This form of therapy is of greatest benefit when the disease is new. Later, when fibrosis is marked, the results are poor. However, eventually the swelling of the glands returns again and again, and a fatal termination is inevitable. It had been noticed that enormous lymphomatous masses may disappear subsequent to an intercurrent disease, such as erysipelas. On this basis an unfiltered mixture of erysipelas and prodigiosus cultures (Coley's) has been injected with good results, probably because of the induced fever.

The duration of the disease is variable. Rarely there may be an acute termination. In the average case the condition lasts from one to two years. When the disease is chronic, it may last many years.

Dr. Arnold DeVeer prepared the pathologic material and chose the most representative parts for photography.

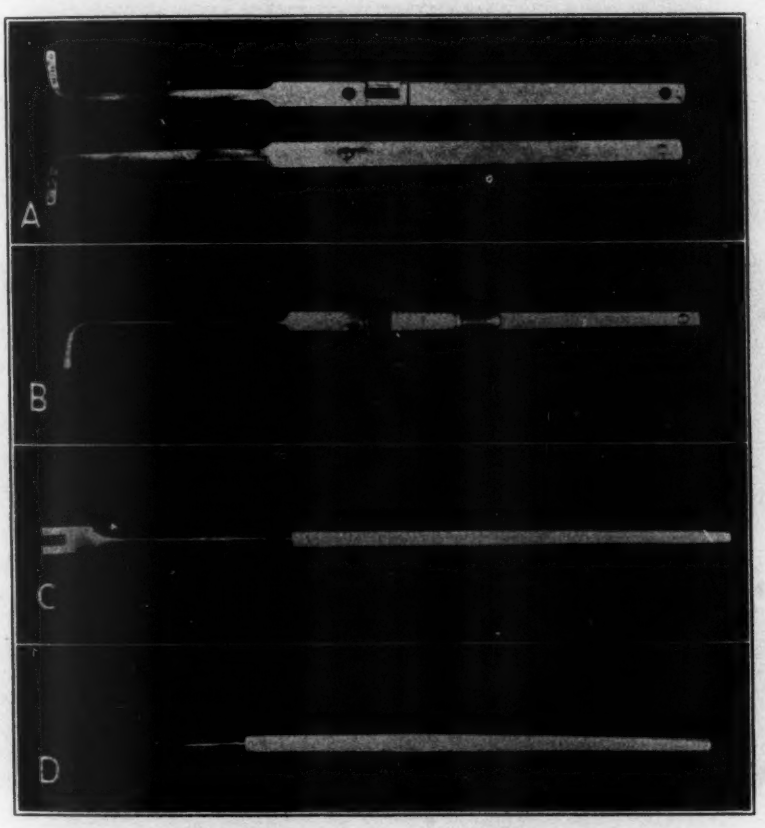
Clinical Notes

NEW INSTRUMENTS FOR OCULAR OPERATIONS

EDWARD RICHARD GOOKIN, M.D., WASHINGTON, D. C.

Description of three instruments which I have completed recently for use at operations on the eye are presented.

The first of these, the clamp and squint hooks, consists of three instruments in one. The squint hooks are used individually but may be



A, the clamp and squint hooks. *B*, the two instruments combined to make the muscle clamp. *C*, the needle guide. *D*, the improved spatula.

combined to make the muscle clamp. The latter makes any operation on a muscle much more simple, and the cost is less than that of instruments previously used.

The second instrument is a needle guide for the purpose of preventing any laceration of tissue during the process of suturing. The guide is pressed against the tissue by an assistant, and the needle and suture are drawn through the opening after the plan utilized in the modern sewing machine.

I also find that the guide is handy in suturing during plastic work on the skin.

The third instrument is an improved spatula, which I find better than other instruments for replacing an iris following extraction of cataract, iridectomy and other operations. I have also used it frequently for raising a pterygium from tissue below; with the spatula held in one hand, the operation can be completed with scissors held in the other hand.

These instruments are manufactured by E. B. Meyrowitz Surgical Instruments Co., Inc., New York.

ARACHNODACTYLY

Report of a Case

TELFORD I. MOORE, M.D., SPOKANE, WASH.

The case of arachnodactyly reported here is interesting because the condition occurs singly in a perfectly normal family (3 siblings) and because of the train of events leading to the diagnosis.

Photographs of the patient.

J. B., aged 6 years, was brought in for examination as required for admission to the state school for the blind. He had been examined at the age of 4 by an oculist (now deceased), who after several attempts to improve the extremely poor vision gave the mother a discouraging prognosis, and nothing was done.

External examination of the eye showed that the patient's far point grossly was about 3 inches (7.6 cm.). The lids, the position of the eyes, conjunctiva, the lacrimal apparatus and the tension on palpation were normal. The pupils were small and irregular. They reacted sluggishly to light and in accommodation. The irides were both tremulous. It was impossible to dilate the pupils more than 3 mm. with any of the common mydriatics, including benzedrine.

Slit lamp examination showed the corneas to be clear. The anterior chambers had normal depth and negative aqueous rays. The irides showed normal pigmentation, but there was definite atrophy of the dilator fibers. The lenses could be seen only in the pupillary area and appeared clear.

Ophthalmoscopically, only a good red reflex was obtained. No details could be elicited, even with the subsequent refraction.

Retinoscopic examination was most difficult; at 0.2 meter about a —38.00 sph. was suggested for each eye. This correction was tried for two weeks with the most dramatic change in the patient. At the time of writing he is in the first grade of the public school and is doing good work. Subsequent tests after he learned a few letters revealed vision to be about 20/100 in each eye with the foregoing correction.

COMMENT

Since the most comprehensive article of Burch [1] in 1936 there has been little added to the bibliography of this interesting condition. The accompanying photographs of the patient aid in establishing the diagnosis. The ocular findings fall in line with those previously reported. The usual finding of congenital heart disease was present in this case. The present plans call for a discission and linear extraction of both lenses.

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1. Burch, F.: Association of Ectopia Lentis with Arachnodactyly, Arch. Ophth. **15**:645-679 (April) 1936.

Ophthalmologic Reviews

EDITED BY DR. FRANCIS HEED ADLER

UNILATERAL PAPILLEDEMA

ITS SIGNIFICANCE AND PATHOLOGIC PHYSIOLOGY

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Although much of the ophthalmic literature deals with papilledema, its unilateral occurrence is mentioned only in widely scattered papers. Unilateral involvement is relatively rare but is nevertheless important and presents a difficult diagnostic problem. When the condition is bilateral certain causes are almost automatically excluded. Many additional factors which complicate the diagnosis must be taken into consideration when the condition is limited to one eye. The term choked disk is assiduously avoided in this paper, because it is often taken to include papillitis or optic neuritis, an entity having a different causation, different pathologic characteristics and symptoms and, to a lesser extent, a different appearance and different sequelae. In their early stages the differentiation of the two conditions may be difficult or impossible. Since a clear understanding of the two conditions is important, for reasons which will be given later, a brief summary of their chief characteristics will be presented here.

In papilledema there is considerable elevation of the nerve head; the arteries may be smaller than normal and the veins enlarged, with great disproportion between the two. There are usually hemorrhages in the retina. Vision may be normal over a long period. The nerve fibers remain clear longer, and the physiologic cup usually persists until the condition is well advanced. Histologically, there is an infiltration which is at first a simple mechanical edema, but if the condition continues, more and more cellular infiltration occurs. The most frequent cause of papilledema is increased intracranial pressure. In optic neuritis, on the other hand, there usually is little if any elevation of the disk.

From the Department of Ophthalmology of the Hospital of the University of Pennsylvania.

Thesis submitted to the faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Master of Medical Science (M.Sc. [Med.]) for graduate work in ophthalmology.

The arteries show little change, and the veins are broad and tortuous. Hemorrhages in the retina are not often present. The vision is usually much impaired from the beginning. The nerve fibers become opaque much more rapidly, and the optic cup is soon obliterated by an exudate. The visual field often shows a central scotoma, while in papilledema there are usually only an enlarged blindspot and slight concentric contraction. Histologically, papillitis is characterized by hyperemia, which accounts for the marked redness of the disk. There is some swelling of the tissues due to an exudate, which is usually serous and plastic or fibrinous and purulent. The latter may change the color to a dull grayish or grayish red tint. Among the more common causes are: general and focal infections, metabolic diseases, toxemias and poisoning (Troncoso). There are, of course, other differential points, and those cited previously could readily be amplified, but this has not been done for the sake of brevity. There are many theories as to the pathogenesis of papilledema. These are of no concern here except in so far as they may throw some light on the factors which limit the papilledema to one eye.

The causes of unilateral papilledema may be classified as follows: ocular and extraocular. The latter may be further subdivided into: (*a*) orbital, (*b*) intracranial and (*c*) general systemic causes. Cases in which one eye is incapable of being affected by papilledema will be discussed under pathologic physiology.

OCULAR CAUSES

Ocular causes include those etiologic factors which are located in the globe or act directly on the globe. The most important factor in this group is reduced intraocular tension. Papilledema due to decreased ocular tension has been observed clinically many times. Elschnig reported a case of keratomalacia with perforation of the cornea in 1902. He described the microscopic appearance of the disk as "identical to that of papilledema due to brain tumor." Similar cases in which papilledema followed perforation of one sort or another, and histologic confirmation was made, have been reported by Stock in 1903, by Fuchs in 1904 and 1928, by Kampherstein in 1904, by Gilbert in 1910, by Behr and by Inouye in 1912 and by others. A close analysis of these cases does not convince one, however, that inflammation might not have been present. The degree of papilledema in such cases may be high. Schieck reported a case in which as a result of a perforating wound a small fistula remained at the limbus. There were no inflammatory signs of any kind. The disk showed an elevation of 4 D. After closure of the fistula by a plastic operation, with resultant increase in the intraocular tension, the swelling disappeared in several weeks. Scardapane

reported 2 cases of perforation of the cornea with subsequent papilledema. In these cases the spinal fluid pressure was elevated. He attributed this elevation to an overproduction of spinal fluid by choroid plexuses irritated by toxins passing from the eye along the optic nerve to the cranial cavity. There is little to substantiate such a theory. Perforation need not necessarily take place in the anterior segment of the eye. Knapp reported a case of retinal detachment in which a Gonin operation was done, which was followed by a swelling of the nerve head amounting to 2 D. In discussing Knapp's paper, Vogt mentioned his own repeated observation of this complication. External trauma without perforation may also bring about a sufficient decrease in the intraocular tension. Polanyi recorded a case of unilateral edema of the nerve head following a nonpenetrating blow. The eye was soft, and the disk was elevated 2 D. On the eighteenth day there was no trace of swelling, and the intraocular tension was 40 mm. of mercury. Polanyi expressed the belief that the hypotension was caused by a disturbance of the ciliary epithelium and that the subsequent hypertension was due to a later irritative reaction with resultant increased secretion. Eppenstein reported a case of glaucoma in which vibratory massage was the only treatment. Seven days after treatment was initiated there were hypotension and a swelling of 2 D., which increased somewhat, then disappeared seven days later without treatment, owing to a recurrent elevation of intraocular tension. Eppenstein expressed the belief that the edema was due to the pressure exerted by the normal tension of intracranial fluid. Carle described a similar case in which papilledema resulted after a sudden reduction in tension due to the use of miotics. Several cases of lowered intraocular tension with papilledema due to phthisis bulbi have been reported by van den Borg. The condition in 1 case followed an attack of measles and in the other tuberculous iridocyclitis and scleritis. In both cases a diagnosis of true papilledema was made on the basis of the histologic studies, but one is justified in questioning the accuracy of the observations.

Papilledema has been produced experimentally by a reduction in the intraocular tension by trephining. Gilbert produced papilledema in a series of rabbits, and Kyrieleis repeated the work with a series of dogs and another series of rhesus monkeys. In these a true papilledema resulted in the absence of any inflammatory reactions, and the author made a thorough histologic study of the specimens. He expressed the belief, however, that papilledema produced in this manner is not like that seen in increased intracranial pressure. He also was of the opinion that it is not the typical sharply marginated "button" or "mushroom" type. The fact that the work was done with animals may account for this.

The only intraocular cause so far described here is reduced intraocular tension. This may be due to perforation. In these cases papillitis cannot be positively ruled out, because infection may have been present. Those cases in which the causative factor was nonperforating trauma or medication strongly suggest that papilledema can be due to lowered intraocular pressure.

CASE 1 (reported by permission of Dr. W. E. Fry).—N. H., a man aged 49, was first seen in February 1935. At that time the tension (Schiötz) was 33.5 mm. of mercury in the right eye and 51.5 mm. in the left eye. The visual fields were characteristic of glaucoma. Examination of the fundi showed in the right eye slight indentation of the disk at the temporal border and in the left eye deep cupping of the disk, typical of glaucoma. Vision in the right eye was 6/5; that in the left eye, with correction, was limited to perception of hand movements. A diagnosis of bilateral glaucoma was made. The patient was treated medicinally until August 1935, at which time an Elliot trephine operation was done on both eyes. On September 5 the tension (Schiötz) in the right eye was 7 mm. of mercury and in the left eye 8 mm. Vision in the right eye was 5/7.5; that in the left eye was 3/100 with correction. On October 17 the vision in each eye was the same as on September 5. Examination of the fundi showed an oval disk and no cupping in the right eye and an atrophic disk and well marked cupping in the left eye. On December 24 vision in the right eye was 5/4; that in the left eye was 1/100 with correction. The tension (Schiötz) in each eye was 7 mm. of mercury. The patient was not seen again until Jan. 27, 1938, at which time vision in the right eye was 6/9; that in the left eye, with correction, was limited to perception of hand movements. Examination of the fundus of the right eye showed the margins of the disk to be hazy. The disk appeared edematous but not elevated. The fundus of the left eye appeared as before. On March 11 vision in the right eye was 6/12; that in the left eye, with correction, was limited to perception of hand movements. Examination of the fundus of the right eye showed elevation of the disk of from 1.5 to 2 D. The edema extended out from the disk to the nasal margin of the macula. There was no change in the fundus of the left eye. Tension on palpation was very low in each eye. On March 21 vision in the right eye was 6/12 with correction. There was no change in the vision in the left eye. The fundus of the right eye showed elevation of the disk of 1 D. Tension was still extremely low.

The patient had no signs or symptoms of hypertension. There were no signs of inflammation, and although the elevation was relatively small, there was definite edema of the nerve head and surrounding tissue. The papilledema was probably due to the lowered intraocular tension. No papilledema developed in the other eye because the nerve was atrophic. As Marchesani pointed out, the glial connective tissue present in atrophic nerves prevents papilledema.

EXTRAOCULAR CAUSES

(*a*) *Orbital Causes.*—The most important orbital causes of unilateral papilledema are neoplasms of any of the structures comprising or contained in the orbit. Such new growths may be of any sort, and

the literature contains reports of various types, including sarcoma of the orbital bones (Rumjantzewa), osteofibroma (van der Hoeve), myeloma (Tahano), cavernous angioma, endothelioma, melanoma (Ewing) and many others. Pfingst reported a case of unilateral papilledema with exophthalmos due to an aneurysm of the ophthalmic artery, and Teulières described 2 cases due to ecchinococcus cysts. Heine studied a case of Mikulicz' disease in which bilateral exophthalmos and unilateral edema of the nerve head were present. An orbital phlegmon may bring about the same result (Kljacko). Tumor of the optic nerve is another cause of unilateral papilledema (Heuss). Grafowa and Mikulinska described a case in which the lower half of the disk was edematous and elevated 3 D., while the upper half was atrophic and flat. Histologic examination showed a partial infiltration of the nerve by a myofibrosarcoma, resulting in atrophy of one half of the nerve fibers due to pressure from thickened septums. The other half of the nerve was distended by lymph in the intercellular spaces. Sinusitis is included in this group of causes. In empyema of a sinus the walls may bulge into the orbit or may cause inflammation of adjacent structures. Belgeri and Arana reported a case of unilateral edema of the nerve head due to sinusitis. When drainage was reestablished by the use of a spray containing a solution of cocaine hydrochloride and epinephrine hydrochloride there was immediate regression of the edema, with sudden restoration of normal vision. Unilateral papilledema in a case summarized by Worms and Chams was attributed to syphilitic involvement of the periorbita and bones. In cases such as the last two papillitis must be carefully excluded.

Case 2 (service of Dr. T. B. Holloway).—R. S., a woman aged 26, was admitted to the hospital on March 12, 1933. The chief complaint was blurred vision in the left eye. Ten days before admission the patient awoke one morning with severe pain in the region of the left eye and the forehead. Vision in the left eye was blurred, the blurring being most marked in the lower temporal field. There was a past history of frequent colds, sinusitis and sore throat. The tonsils and adenoids had been removed ten years previously. Physical examination gave negative results except for thickening of the left middle and inferior turbinates due to pus in the left sphenoethmoid region. Roentgen examination showed bilateral ethmoiditis. There was a slight increase in the density of both antrums. The optic foramens were normal. Ophthalmic examination showed vision of 6/5—2 in each eye. External examination gave negative results. The fundus of the right eye was normal. The fundus of the left eye showed papilledema of 3 D. On March 20 the visual field of the right eye was normal. The field of the left eye showed slight concentric contraction and an enlarged blindspot. The picture was suggestive of a defect in the left inferior nasal quadrant. Ophthalmoscopic examination of the right eye gave negative results. There were many opacities of the vitreous of varying size in the left eye, with numerous areas of exudates and diffuse hemorrhages. The papilledema was slightly increased. On March 21 the visual field of the right eye was normal. The concentric con-

traction in the left eye was more marked, and the quadrant defect was increasing in size. Ophthalmoscopic examination showed no change. On March 24 sphenoethmoidectomy on the left side was followed by immediate improvement and total regression of the papilledema in six days.

The papilledema in this case was undoubtedly due to ethmoiditis. At operation a considerable quantity of pus was evacuated. Inflamed ethmoid cells may cause pressure on the optic nerve, either directly or indirectly by inflammation or edema of adjacent structures.

CASE 3 (reported by permission of Drs. Francis Heed Adler and Francis C. Grant).—G. D. S., a girl aged 12 years, was admitted to the hospital on June 11, 1937. The chief complaint was pain in the left orbital region of three or four months' duration, beginning occasionally in the morning. There was a gradual increase in severity and frequency, the pain never lasting more than a few minutes, with intervals of freedom. Vision in the left eye had gradually been blurring for one month before the patient's admission. Physical examination showed a few tags of tonsil tissue remaining. Many glands were palpable in the neck. Ophthalmic examination on June 8 showed vision of 6/6 in the right eye and 6/9 in the left eye. The visual field of the right eye showed concentric contraction and an elongated blindspot. The visual field of the left eye showed concentric contraction, which was marked for red. The field for red cut to the midline on the temporal side. The blindspot was enlarged. The fundus of the right eye was normal; that of the left eye showed papilledema of 4 D. and a few hemorrhages. External examination did not reveal any exophthalmos. The left corneal reflex was slightly less than the right. Roentgen examination of the skull gave negative results. On June 15 ophthalmic examination showed the right eye to be normal. There were papilledema of 2 D. and a few hemorrhages in the left eye. The visual fields were similar to those seen at the previous examination. An encephalogram made on June 17 was normal. On June 29 ophthalmic examination gave entirely negative results. Vision was 6/6 in the right eye and 6/6—1 in the left eye.

In view of the fairly good vision and the characteristics of the changes in the visual fields and the fundus, a diagnosis of papilledema was made. This case is included in this group because the enlarged glands in the neck were suggestive of a focus of infection in the sinuses, although at that time no definite evidence of sinus disease was found. Furthermore, the papilledema subsided without treatment.

CASE 4 (services of Drs. J. C. Gittings and Francis C. Grant).—M. G., a girl aged 11 years, was admitted to the hospital on June 21, 1937. The chief complaint was fainting spells since September 1936, followed by frontal headaches and precordial pain. Weekly attacks occurred up to March 1937. There were no attacks until May 1937, then they increased in frequency. Physical examination showed slight thickening of the mucous membrane in the region of the maxillary and ethmoid sinuses. There was partial obstruction of the left nasal passage. Enlarged glands were palpated in the anterior and posterior triangles of the neck. Ophthalmic examination showed vision of 6/9 in each eye. The fundus of the right eye was normal. Examination of the fundus of the left eye revealed papilledema of 4 D. The left pupil was slightly smaller than the

right. The visual field of the right eye was normal; that of the left eye showed slight concentric contraction and an enlarged blindspot. The patient was removed from the hospital by her parents on June 23. She was readmitted on July 22 because of recurrent fainting spells and convulsive seizures. Physical examination gave the same results as on the first admission. Roentgen examination of the skull gave negative results. An encephalogram made on July 23 was normal. Ophthalmic examination on July 26 showed vision of 6/9 in the right eye and 6/12 in the left eye. The fundus of the right eye was normal. The papilledema in the left eye had subsided to 1 D.

In this case a diagnosis of papilledema was made because of the characteristics of the visual fields, the fundus pictures and the relatively small impairment of vision. Nevertheless, papillitis cannot be definitely excluded. The etiologic factor here was probably the same as that in the preceding cases. The convulsive seizures were thought to be of psychic origin.

(*b*) *Intracranial Causes.*—The most common intracranial cause of unilateral papilledema is tumor. A tumor associated with edema of one nerve head may be located anywhere. The literature includes reports of cases of frontal tumor (Ballado and Adrogué, Foster Kennedy, Haitz, Herrmann, Marchesani, Mylius, Schmelzer, Thies and many others), of chiasmal tumor (Sørensen, Christiansen); of tumor of the sphenoid ridge (Alpers and Groff), of tumor of the cerebellopontile angle (Brückner, Hagens, van der Hoeve and others), of cerebellar tumor (Herrmann) and of tumor of the sella turcica (Vincent). Many other tumors in various locations, too numerous to mention, are referred to in the literature. Bruttin recorded an aneurysm of the internal carotid artery associated with unilateral papilledema. Loeb described a case of fracture of the skull in which this complication was present, and Kraft, a case of diffuse melanosarcoma involving all the meninges and penetrating into the smallest crevices of the skull and brain. For reasons to be discussed later, any space-taking lesion or any disease which raises the intracranial pressure may result in unilateral papilledema. One other cause, inflammation, might be mentioned here. Decking described a case of unilateral edema of the nerve head following the injection of alcohol into the gasserian ganglion. The patient also presented signs suggestive of a tumor of the pontile angle, so that the exact cause of the edema is not certain but may have been the result of a localized meningitis. Unilateral involvement is occasionally observed in meningitis.

Case 5 (service of Dr. Francis C. Grant).—J. D., a man aged 55, was admitted to the hospital on July 25, 1936. The chief complaint was headache behind the left eye of increasing severity for eight weeks. There was gradual extension to the back of the right eye. Personality changes occurred over a period of one year. The patient was stuporous on admission. Physical examination gave negative results. The cerebrospinal fluid pressure was 24 mm. of mercury. The

laboratory studies gave negative results. Roentgen examination showed erosion of the right frontal bone. Ophthalmoscopic examination of the right eye showed papilledema of 2 D. There was slight engorgement of the veins in the left eye but no papilledema. On July 25 a bone flap was turned down in the right fronto-parietal region, and a subcortical tumor was found occupying the posterior part of the right temporal lobe and the anterior part of the right parietal lobe low down below the level of the sylvian fissure. A diagnosis of blastoma multiforme was made.

CASE 6 (service of Dr. C. H. Frazier).—S. P., a man aged 47, was admitted to the hospital on Oct. 26, 1935. The chief complaints were headaches of increasing severity, of one month's duration, more marked in the right frontal region; increasing general weakness; apathy; impaired memory, and tinnitus on the right side. The blood pressure was 150 systolic and 80 diastolic. Physical examination revealed anosmia, a decrease in the tendon reflexes on the left side and weakness of the left side of the face. Ophthalmic examination showed a yellowish secretion in the conjunctival sac of the left eye. There was 4 D. of papilledema in the fundus of the right eye. The margins of the disk of the left eye were hazy, but there was no papilledema. Roentgen examination of the skull gave negative results. On October 31 a transfrontal craniotomy revealed a tumor in the right frontotemporal region, an astrocytoma.

CASE 7 (service of Dr. C. H. Frazier).—W. C., a man aged 55, was admitted to the hospital on April 22, 1931. The chief complaints were vertigo; unsteadiness on standing or walking, slowly increasing since the onset in 1926; tinnitus in the left ear; falling to the right, and dull headaches. The blood pressure was 120 systolic and 80 diastolic. There was a positive Romberg sign. Ophthalmic examination showed lateral nystagmus when the patient turned the eyes to the extreme left. The visual fields were normal. Examination of the fundus of the right eye showed papilledema of 2.5 D. The fundus of the left eye was normal. Laboratory and roentgen studies gave negative results. A diagnosis of a tumor of the left cerebellopontile angle was made. Suboccipital craniotomy on May 9 revealed a neurofibroma of the eighth nerve.

CASE 8 (services of Drs. T. B. Holloway and C. H. Frazier).—M. B., a girl aged 19, was admitted to the hospital on Sept. 25, 1935. The chief complaints were blurred vision in the right eye and vomiting on awakening for one month. On August 29 the patient had a fainting attack, followed by rigidity of the arms and partial loss of vision in the right eye. On September 22 she had an attack of unconsciousness, followed by a severe frontal headache. The blood pressure was 185 systolic and 100 diastolic. The patient suffered from somnolence. Physical examination revealed impairment of the muscle tone, hypoactive reflexes on the right side, numbness of the right fourth and fifth fingers and loss of sense of smell. Laboratory studies gave negative results. Roentgen examination showed increased intracranial pressure and erosion of the posterior clinoid processes. On ophthalmic examination the margins of disk of the right eye were found to be hazy; the color was yellowish but the disk was not atrophic. The right eye deviated outward 30 degrees, and there was amblyopia. Papilledema of 5 D. was present in the left eye. On October 7 a ventriculogram showed a tumor involving the third ventricle and obstructing the anterior portion. Right transfrontal craniotomy revealed a tumor of the third ventricle, an astrocytoma, blocking the outlet of the right lateral ventricle.

CASE 9 (reported by permission of Dr. Francis C. Grant).—E. G., a woman aged 40, complained of visual disturbance for four months, attacks of diplopia lasting from ten to fifteen minutes and occasional blurring of vision. Physical examination revealed impairment of the sense of smell on the right side, slight weakness of the lower right side of the face and deviation of the tongue to the right. Ophthalmic examination showed vision of 6/12 in the right eye and 6/9 in the left eye, with horizontal nystagmus on gaze to the left. The fundus of the right eye was normal. There was papilledema of 5 D. in the left eye. The visual fields were normal. A ventriculogram, made on Feb. 15, 1933, showed the ventricles displaced to the left. The right ventricle was deformed, and the anterior right horn was absent. Right transfrontal craniotomy revealed a tumor of the right sphenoid ridge, a fibroblastoma.

(*c*) *General Systemic Causes.*—Unilateral papilledema may theoretically occur in any disease which produces increased intracranial pressure. The mechanism will be discussed under the pathologic physiology. Adler reported a case of multiple sclerosis in which there was unilateral edema of the nerve head lasting for three months. It then disappeared completely and was followed by pallor in the temporal region. Shortly thereafter the same process was repeated in the other eye over the same period of time. The case is unusual, because of the unilaterality of the condition and also because papilledema is usually evanescent in multiple sclerosis. Brazeau described a case of chlorosis with unilateral involvement. Syphilis is probably the most frequent cause in this group, although there are no statistics to support such a belief. The papilledema due to systemic disease owes its unilaterality in most instances to localized changes in the eye, orbit or cranium.

CASE 10 (services of Drs. Francis C. Grant, John H. Stokes and Francis Heed Adler).—M. D., a man aged 27, was admitted to the hospital on May 6, 1937. The chief complaint was marked diminution of vision in the left eye of three weeks' duration. The patient had an initial syphilitic lesion in January 1937. He was treated at another hospital and received four weekly injections of an arsenical preparation. No therapy was given during February and March. During the first week in April the patient received one intravenous injection of some drug, followed by diminished vision in the left eye. He then went to a second hospital, where he was said to have had papilledema of 4 D. in the left eye and slight papilledema in the right eye. While there, he was suspected of having a tumor of the brain and was sent to the Hospital of the University of Pennsylvania. Physical examination gave negative results. The Wassermann reaction of the blood was strongly positive. The spinal fluid gave a negative reaction to the Wassermann test; the protein content was 75 mg. per hundred cubic centimeters, the cell count 10 and the colloidal gold curve 0122221000. External examination of the eye gave negative results. Examination of the fundus of the right eye showed the outlines of the disk to be blurred and the disk to be slightly elevated, possibly 1 D. There was papilledema of 4.5 D. in the fundus of the left eye, with many hemorrhages and a macular star figure. Vision was 6/9—2 in the right eye and 1/60 in the left eye. The visual field of the right eye showed slight concentric contraction and an enlarged blindspot; that of the left eye showed slight concentric contraction and marked enlargement of the blindspot. The patient

was put on a course of antisyphilitic therapy. On October 19 examination of the fundus of the right eye showed the disk to be still slightly elevated, possibly 0.5 D. The fundus of the left eye showed papilledema of 3 D., slight edema of the macula and a slight pigmentary disturbance. Vision was 6/12—2 in the right eye and 6/150 in the left eye. The visual field of the right eye showed concentric contraction; the field of the left eye was similar.

This case is included because the papilledema of the right eye was negligible after antisyphilitic therapy. There is some doubt as to whether the process in the left eye was pure papilledema because of the low vision. This, however, may be accounted for by the fact that the edema extended out to the macula. The visual fields were more suggestive of papilledema than papillitis, although the latter cannot be definitely excluded. The fact that only one nerve head showed much edema could be accounted for by a localized arachnoiditis around the right optic foramen, which prevented the cerebrospinal fluid from entering the intervaginal space of the right optic nerve.

CASE 11 (service of Dr. Francis C. Grant).—V. C., a man aged 29, was admitted to the hospital on Feb. 1, 1937. His chief complaints were headaches of one month's duration, occasional nausea and vomiting of increasing frequency and severity and, later, failing memory for recent events, loquacity, vertigo and blurred vision in the left eye. Physical examination showed slight weakness of the mouth on the right side and hyperactive patellar reflexes, more marked on the right. On ophthalmic examination it was found that the pupils did not react to light or in accommodation and that the corneal reflexes were hyperactive. Examination of the fundus of the right eye showed possible slight edema of the nerve head but no measurable elevation. Papilledema of 3.5 D. was present in the left eye. The visual fields showed a right homonymous superior sector cut and either a binasal inferior sector cut or possibly a left homonymous inferior defect with a reentering angle about 15 degrees left of the midline, breaking through to the blindspot in the left eye and also catching the lower nasal field in that eye. The blindspots were greatly enlarged. Vision was 6/9 in the right eye and 3/60 in the left eye. The cerebrospinal fluid pressure was 27 mm. of mercury. The Wassermann reaction of the spinal fluid was negative, and the colloidal gold curve was 1122244444. Roentgen examination revealed a possible tumor of the right sphenoid ridge. On February 27 a ventriculogram showed internal hydrocephalus with evidence of a block in the proximal portion of the iter. On suboccipital craniotomy tonsils of cerebellum were found adherent to the opening of the fourth ventricle. The tonsils and vermis were freed of adhesions. Sections of tissue were taken from about the opening of the fourth ventricle. Microscopic examination revealed syphilitic meningitis. Necropsy disclosed syphilitic basilar arachnoiditis.

The mechanism in the case, which limited the papilledema to one eye, was probably the same as that suggested in the preceding case.

CASE 12 (reported by permission of Dr. Francis Heed Adler).—B. M., a man aged 45, was first seen in December 1926. Vision in each eye was 6/6. The fundi were normal. On June 27, 1931, the patient had an attack of glaucoma in the right eye. The tension (Schiötz) in the right eye was 60 mm. of mercury

and in the left eye, 13 mm. The tension was controlled with miotics until March 12, 1935, when the Elliot trephine operation was performed on the right eye. On March 27 the tension (Schiötz) in the right eye was 9 mm. of mercury and in the left eye 18 mm. About this time signs and symptoms of an arterial hypertension began to develop. The intraocular tension in the right eye began to drop steadily, and on June 14 it was 5 mm. of mercury in the right eye and 17 mm. in the left eye (Schiötz). No ocular signs of hypertension developed until October 1, although the patient was seen at least once a month. At that time the fundus of the right eye showed arteries deeply indenting the veins, which were markedly overfilled, and several small points, which were suggestive of hemorrhages. The fundus of the left eye was normal. The tension (Schiötz) in the right eye was very low; that in the left eye was 18 mm. of mercury. The blood pressure was 180 systolic and 100 diastolic. On October 7 there was no change except for a definite hemorrhage on the right disk. The left eye was normal. On December 5 the tension in the right eye was extremely low, and the eye was soft. The tension (Schiötz) in the left eye was 21 mm. of mercury. Examination of the fundus of the right eye showed many hemorrhages on the disk, marked arteriovenous compression and a definite edematous appearance. The fundus of the left eye showed slight arteriosclerotic changes, normal for the patient's age; otherwise the fundus was normal. On Jan. 1, 1936, the tension in the right eye was extremely low on palpation; that in the left eye (Schiötz) was 25 mm. of mercury. The fundus of the right eye showed papilledema of from 2.5 to 3 D., many hemorrhages and cotton wool exudates and marked arteriovenous compression. The fundus of the left eye was normal. On October 29 the tension (Schiötz) in the right eye was 7 mm. of mercury and in the left eye 21 mm. There was little change in the fundi. The blood pressure was 190 systolic and 125 diastolic. On Jan. 7, 1937, the tension (Schiötz) in the right eye was 11 mm. of mercury and in the left eye 21 mm. There were no hemorrhages or exudates in the fundi and little edema of the nerve heads. On March 12 the tension (Schiötz) was 12 mm. of mercury in the right eye and 25 mm. in the left eye. Examination of the fundus of the right eye showed tortuous vessels and an increase in light streaking. On January 5 the blood pressure was 210 systolic and 130 diastolic. On palpation the tension was normal in each eye. The fundi showed no change. On March 25 the blood pressure was 190 systolic and 120 diastolic. The tension (Schiötz) was 14 mm. of mercury in the right eye and 23 mm. in the left eye. The fundus of the right eye showed well marked arteriosclerosis. The disk had a good color, and there was no papilledema, hemorrhages or exudates. The fundus picture of the left eye was the same.

The exciting cause for the papilledema in this case was probably the lowered intraocular pressure. It is interesting to note that although the patient had all the signs and symptoms of hypertension, marked changes did not develop in his left eye. The arterial hypertension steadily increased, but as soon as the intraocular tension of the right eye increased, the papilledema, cotton wool exudates, hemorrhages and marked venous dilatation disappeared. One school of thought believes that retinal changes of this type seen in patients with arterial hypertension are definitely indicative of a serious prognosis and that only a small percentage of such persons survive for more than a few years. There are many persons who have shown such changes and are still in fair health

many years later. It is within reason to say that in this case the retinal changes which accompanied arterial hypertension were markedly accentuated by the low intraocular tension. It is well known that such patients may show remissions. The disappearance of the retinal changes of the right eye was probably not an ordinary remission for two reasons. In the first place, the arterial tension rose constantly. In the second place, the disappearance occurred only after an increase in the intraocular tension of this eye. Moreover, no similar change took place in the left eye. There is, therefore, a direct relationship between the degree of retinal change and the ocular tension. It is probable that the evaluation of any case in which there is marked arterial hypertensive changes may be considerably more accurate if the intraocular tension is taken into account. As far as I know, this point has hitherto not been mentioned.

PATHOLOGIC PHYSIOLOGY

In order to understand the mechanism of unilateral papilledema, one must have a clear conception of the physiologic changes which may take place. The most widely accepted theory of the cause of papilledema is probably that of Paton and Holmes. According to these authors, the primary cause of the edema is pressure on the vena centralis in the intervaginal space. Fry studied an extensive series of cases of papilledema by means of serial sections and found ample evidence to show that the compression of the central vein of the retina takes place either along the side of the nerve or in the subarachnoid space. In another study he found that there is considerable variation in the course of the central artery and vein. He stated: "The relatively long course of the vein in the subpial and intervaginal space . . . would favor compression of this vessel by increased pressure of the fluid within the dura in cases of increased cerebrospinal fluid pressure, and hence be of importance in the production of papilledema." He was able to show that "the secondary cause of papilledema is a forward pressure of fluid within the optic nerve produced in all probability by the infiltration of spinal fluid under increased pressure in the perivascular lymph spaces." One may then say that papilledema is at least in part due to changes in the normal circulation through the central retinal vein and that unilateral papilledema may be the result of factors influencing the circulation through one central retinal vein. The simplest interference resulting in unilateral papilledema is pressure directly on the vein, such as may arise from intraorbital causes, tumors, cysts, aneurysms and periostitis. In such cases there are often other concomitant symptoms and signs, such as exophthalmos and involvement of the orbital nerves, which aid in diagnosis.

The mechanism in unilateral papilledema due to an increase in intracranial pressure is somewhat more complicated. First of all one disk may be free from papilledema because no fluid, or only a small amount, gains access to the intervaginal space from the cranial vault. This may be due to arachnoiditis or some other localized process, such as tumor growth in the region of the optic foramen, which blocks the exit of fluid from the skull. Moreover, as Marchesani and others have pointed out, papilledema usually occurs only in vital nerves. In 1 of his cases there was edema only on the nasal side of the disk and none in the atrophic temporal portion. The same author described a second case in which there was papilledema of several diopters in one eye as a result of increased cerebrospinal fluid pressure. The second eye showed no papilledema. Ophthalmoscopic examination showed 20 D. of myopia and an atrophic nerve head. A careful necropsy and histologic studies showed typical papilledema on the one side and only a faint suggestion thereof in the atrophic nerve. These two factors, atrophy and blockage at or near the optic foramen, are of importance in the syndrome described by Gower, Paton, Uthoff, Traquair, Foster Kennedy and others. In this syndrome of tumor of the frontal lobe there is atrophy of the optic nerve on the side of the tumor and papilledema on the other side. It must not be assumed, however, that given a case of tumor of the frontal lobe with atrophy on one side and papilledema on the other that one is necessarily confronted with a tumor located on the side of the atrophic disk. Dowman and Smith reported a case in which there were papilledema on the right side and atrophy on the left side. The tumor was located in the right frontal lobe. Thies and others have described similar cases. It may be that in these cases there was atrophy of one nerve of long standing due to an entirely different cause. Another explanation must be considered. The increased intracranial pressure may have caused unilateral papilledema at first, which progressed to atrophy. After this, the intracranial pressure steadily rose and caused papilledema in the other nerve. This mechanism will be considered more in detail later.

In the absence of the two aforementioned factors, unilateral papilledema may still occur in intracranial hypertension. As Fry has shown, the central retinal vein may run through the intervaginal space for some distance. If one central vein were exposed to the pressure of cerebrospinal fluid for a greater distance than the other, unilateral papilledema might occur. The longer the course of the vein in the intervaginal space, the less will be the pressure needed to produce papilledema in the corresponding nerve head.

Increased cerebrospinal fluid pressure may result in unilateral papilledema in still another manner. All that is needed is a rise in the

pressure in one central retinal vein. The return venous blood from the ophthalmic veins passes through the two cavernous sinuses, which are joined anteriorly and posteriorly by the annular sinuses. Leaving these, a large volume of blood passes to the junction of the transverse and sigmoid sinuses by way of the superior petrosal sinuses. Some of the blood also passes from the cavernous sinuses downward and posteriorly by way of the inferior petrosal sinuses to the jugular bulb. The sigmoid sinuses run from the junction of the superior petrosal and transverse sinuses to the jugular bulb. The transverse sinuses are fed by the large central sinuses, which drain both cerebral hemispheres, the midbrain and the cerebellum, through the superior and inferior longitudinal and straight sinuses. Swift, in a study of the relation of the cranial sinuses to papilledema, showed how tumors may change the venous pressures. It may be that pressure on the right cavernous and inferior and superior petrosal sinuses could cause a rise in the pressure in the right ophthalmic vein. Pressure on the right transverse sinus could cause a rise in the pressure in the left ophthalmic vein. Thus unilateral papilledema could be produced. Gibbs pointed out how such a disturbance might cause unequal edema in the optic nerve heads in tumors of the brain. In most cases unilateral papilledema due to increased intracranial pressure progresses to bilateral involvement, and it is not unreasonable to presume that in most cases of unequal bilateral papilledema the condition began with involvement of only one disk. It is highly problematic whether interference with circulation of the sinuses alone, in the absence of a generalized increase in intracranial pressure, could cause papilledema, as evidenced by the number of cases of sinus thrombosis in which there was no papilledema (Uhthoff). As Gibbs has pointed out, this theory needs much carefully controlled experimental work. Many factors, such as the rapidity and direction of tumor growth relative to the sinuses, are not taken into consideration here. Moreover, as Swift and others have pointed out, the cranial sinuses vary enormously in size, location and anastomoses. All these factors must influence the development of papilledema. The circulation of the sinuses is probably quickly adjusted to any interference at one point or another, so that this factor by itself is not in all likelihood of cardinal importance.

The physiologic mechanism of unilateral papilledema of ocular origin is more abstruse. According to Sobański and Lauber, an increase in the diastolic venous pressure and its relation to the arterial diastolic pressure in the retina are decisive factors in the production of papilledema. The work of these authors shows that any alteration in the ratio of these pressures, as measured by their methods, beyond 1 : 1.5 always leads to papilledema. It is likely that this relation is somehow or other disturbed in cases of papilledema due to low intraocular pressure. Paton and Holmes, Kyrieleis, Parker and others have shown that the eye with the

lower intraocular pressure shows the greater degree of papilledema in cases of increased cerebrospinal fluid pressure. The lamina cribrosa may be considered as a diaphragm which moves forward with an increase in the intracranial pressure (Fry). In the event that the cranial pressure remains the same, the lamina cribrosa might move forward if the resistance against the normal intracranial pressure were removed, as is the case when the intraocular tension is lowered. The normal lamina cribrosa is convex toward the optic nerve and concave toward the lens. If it is pushed anteriorly, the structures passing through its interstices must be compressed. The vein being more easily collapsible than the artery, because of its thinner walls, would suffer more compression. Such compression would raise the venous pressure, so that edema might result or at least be increased. In an eye in which the pressure had been reduced by means of a cyclodialysis for glaucoma, Sobański and Lauber found papilledema of 2.5 D. The diastolic arterial pressure was 38 mm. of mercury and the diastolic venous pressure 25 mm., a ratio of 1.5 : 1.

SUMMARY

The causes of unilateral papilledema may be grouped under the following headings: intraocular, intraorbital, intracranial and systemic. The last is probably dependent on localized changes in the region of the optic foramen or to a combination with one of the other causes.

In the event of a space-taking lesion the papilledema may not be homolateral and cannot be depended on by itself to determine the side on which the tumor is located.

Patients presenting unilateral papilledema should be subjected to a study, including measurement of the intraocular pressure, exophthalmometer measurement, thorough neuro-ophthalmic examination, spinal fluid studies and roentgen examination of the head, including the optic foramens and the sinuses.

The importance of certain factors which have not received due consideration heretofore is discussed. These are: the relation of intraocular pressure to papilledema, particularly in arterial hypertension, and the yielding of the lamina cribrosa, with direct compression of the vein and elevation of the retinal venous pressure.

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News and Notes

SOCIETY NEWS

Association for Research in Ophthalmology.—The tenth scientific meeting of the Association for Research in Ophthalmology, Inc., will be held on May 16, 1939, at the Coronado Hotel, St. Louis. The following papers will be presented: "Experimental Ocular Hypersensitivity," by Dr. T. E. Sanders, department of ophthalmology, Washington University, St. Louis; "Studies on Surface Epithelium Invasion of the Anterior Segment of the Eye," by Drs. T. L. Terry, J. F. Chisholm and A. L. Schonberg, Massachusetts Eye and Ear Infirmary, Boston; "A Study of Methemoglobin-Producing Organisms in Ocular Inflammations," by Dr. Maynard A. Wood, department of ophthalmology, University of Iowa, Iowa City; "The Relation of Müllers Orbital Muscle to the Pathology of Retrobulbar Tissues Obtained in Experimentally Produced Exophthalmos," by George K. Smelser, Ph.D., department of ophthalmology, Columbia University, New York; "Ocular Reactions of Horses and Rabbits Infected with Strains of Brucella Recovered from Horses with Periodic Ophthalmia," by Dr. E. L. Burky, Robert Redvers Thompson, Ph.D., and Helen D. Zepp, A.B., the Johns Hopkins Hospital, Baltimore; "Staphylococcus Conjunctivitis: Experimental Reproduction with Staphylococci," by Dr. James H. Allen, department of ophthalmology, University of Iowa, Iowa City; "An Immunological Study of Trachoma," by Louis Julianelle, Ph.D., department of ophthalmology, Washington University, St. Louis, and "Vitamin-D Complex in Myopia: Etiology, Pathology and Treatment," by Dr. Arthur E. Knapp, New York.

Oxford Ophthalmological Congress.—The Oxford Ophthalmological Congress will assemble at Keble College, Oxford, on Wednesday evening, July 5, and the meetings will be held on the following Thursday, Friday and Saturday, July 6, 7 and 8.

The Doyne Memorial Lecture will be delivered by Mr. F. A. Williamson-Noble, F.R.C.S., of London, England, and will be entitled "Ocular Consequences of Certain Chiasmal Lesions."

On Thursday morning, July 6, there will be a discussion on orthoptic training. The discussion will be opened by Mr. Frank Law and Mr. Keith Lyle, who will be followed by Miss Sheila Mayou, Messrs. E. B. Alabaster, George Black, H. Campbell Orr, P. Jameson Evans, Bernard Chavasse and O. M. Duthie.

On Saturday morning, July 8, Mr. Harrison Butler will open a discussion on miners' nystagmus.

The following papers have already been promised: "The Latest Principles for Applying Tinted Glass to Industrial and Other Purposes," by Sir Arnold Lawson, of London; "Drusen of the Retina: A Clinical and Pathological Study," by Dr. Bernard Samuels, of New York; "Number Forms," by Mr. P. J. Doyne, of London, and "The Ophthalmic Surgeon's Functional Operative Paresis," by Mr. Basil Graves, of London.

GENERAL NEWS

American Board of Ophthalmology.—The American Board of Ophthalmology will conduct a written examination in various cities in the United States, in Honolulu, Territory of Hawaii, and in Puerto Rico, as well as in Canada, on August 5. Formal application for this examination must be received before July 1. General oral examination for successful candidates will be held on October 7 in Chicago.

For application blanks and information, write at once to the secretary, Dr. John Green, 6830 Waterman Avenue, St. Louis.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Biochemistry

THE PHOSPHATASES OF THE LENS. A. SANTONI, Ann. di ottal. e clin. ocul. **66:** 209 (March) 1938.

An extract of whole beef lens was allowed to react with a standard solution of sodium glycerophosphate. The material was examined for the amount of phosphorus present after deproteinization with trichloroacetic acid, and this amount was compared with the phosphorus in the lens extract alone. Splitting of the phosphate occurred best at p_H 9.2. From 4 to 12 per cent of the phosphate present in the solution was broken down in twelve hours, indicating definitely the presence of phosphatase in the lens. The amount is less than that found in most other tissues.

S. R. GIFFORD.

Blindness

CAUSES OF BLINDNESS, editorial, Brit. M. J. **2:** 796 (Oct. 15) 1938.

The thirty-second annual report of the Northern Counties Association for the Blind presents an analysis of 10,000 cases of blindness, made by the medical subcommittee, of which Dr. Kay Sharp, consulting ophthalmic surgeon, West Riding County Council, is chairman.

Of the 10,000 cases of blindness, 6,406 were due to congenital or undetermined causes, primary cataract accounting for more than one-half and primary glaucoma for one-sixth. The number of cases due to infectious and bacterial causes was 1,791, of which 405 were ascribed to ophthalmia neonatorum and 492 to syphilis, congenital or acquired.

There were 580 cases of blindness due to traumatic and chemical causes, industrial trauma accounting for 262 and nonindustrial trauma for 286.

Eight hundred cases of blindness were ascribed to general disease, the greatest number being due to vascular diseases, including cerebral vascular lesions, and the next greatest number, to diabetes.

Of the 10,000 cases, no information as to cause was obtainable concerning 423.

ARNOLD KNAPP.

Color Sense

BEHAVIOR OF THE COLOR SENSE DURING COMPRESSION OF THE GLOBE. A. SANTONASTASO, Ann. di. ottal. e clin. ocul. **66:** 161 (March) 1938.

When pressure is made on the globe during observation of a colored target, two phenomena occur. First, the color of the object is lost, and as pressure is increased, the object itself is lost to view. The author investigated these phenomena in 10 normal observers with blue, red and green targets observed in natural light and with lights of pure spectral color in the darkroom after suitable adaptation. Observations

for these colors were made not only at the fixation point but at various points on the horizontal meridian, including 40, 25 and 10 degrees on the temporal side and 25 and 15 degrees on the nasal side. The pressure of the dynamometer required to abolish the color and that required to abolish perception of the target were recorded, the difference in the two pressures measuring what the author calls the chromoluminous interval. The results were fairly constant for all the persons examined. The results, in general, were as follows:

1. For the central portion of the retina, less pressure was necessary to obliterate the color in the darkroom than in daylight, while for the peripheral portion of the retina the opposite was the case. This indicates that the peripheral portion of the retina functions better than the central portion in the darkroom, while in daylight the central portion is superior.

2. The chromoluminous interval was greater, especially for red and blue, in the periphery than in the center.

3. When the intensity of the colored stimulus was decreased, less pressure was necessary to obliterate it.

4. In the extreme periphery less pressure was necessary to obliterate the color. This was especially true at the nasal side and with observation in daylight.

5. When the color disappeared during pressure, a slight movement of the target caused it to reappear, as a rule, but this was more uniform if it was moved toward the fixation point. If it was already at the fixation point, a slight movement to either side caused it to reappear, but when high pressures were employed, this sometimes occurred only when it was moved to the temporal side.

For other interesting details and some conclusions bearing on the theories of color vision, the original article must be consulted. Perhaps the most important of these is one suggested by the fact that dark adaptation did not improve the function of the retina for color so far as to increase the pressure required to obliterate color sensation even in the retinal periphery. A bibliography accompanies the article.

S. R. GIFFORD.

Conjunctiva

PRIMARY TUBERCULOUS INFECTION OF THE CONJUNCTIVA. BENALIOUA, Ann. d'ocul. **175:** 746 (Oct.) 1938.

Primary tuberculous infection of the conjunctiva, the existence of which has been demonstrated, is a disease of children and young adults and is seen more frequently in females than in males. It is manifest especially as a unilateral conjunctival pretragal complex, of a sluggish nature, associated with various lesions of the mucous membrane and frequently with numerous caseous glands.

The prognosis of this condition, long considered particularly grave, is in reality favorable, cures occurring without any complication except bacillary migrations, which are without danger and are no doubt conveyed by an erythema. The relatively good prognosis permits primary

tuberculous infection of the conjunctiva to be placed under the same pathogenic classification as visceral tuberculosis and particularly pulmonary tuberculosis.

Treatment of the ocular condition should not be too aggressive, and it is considered much the best plan, as in a primary pulmonary infection, to institute general tonic systemic treatment and to reserve the usual local treatment for the form of slow evolution with a manifest tendency to spontaneous relapse.

A bibliography of four pages accompanies the article.

S. H. McKee.

Fate of Patients with Phlyctenular Disease with Particular Refference to Tuberculosis. A. Ajo, Acta ophth., 1938, supp. 15, p. 1.

This monograph first gives a historical review of ideas which have been held in regard to the etiology and pathogenesis of phlyctenular disease. It then deals with the question of the prognosis of ocular phlyctenulosis with particular regard to the later development of tuberculosis.

In the University Eye Clinic at Helsingfors, Finland, there were 449 patients with phlyctenular disease between 1912 and 1927. The author succeeded in tracing 367 of these patients. He found that 55 had died. Tuberculosis was the cause of death of 35, and for 4 more it was the probable cause, making the mortality rate for tuberculosis 10.62 per cent. This is about double the mortality rate for tuberculosis for persons of the same age group in the general population of Finland.

Of the former patients still living, 100 were thoroughly examined. Fifty were found free from disease. Thirty-nine of the remaining 50 patients showed tuberculous changes. Five showed changes which were probably tuberculous and 6, other pathologic changes. Pulmonary tuberculosis was found in 7 patients. The author concludes that it may not be held that patients with phlyctenular disease will be spared later severe tuberculosis.

O. P. Perkins.

Congenital Anomalies

Aplasia of the Optic Nerves. H. Ridley, Brit. J. Ophth. 22: 669 (Nov.) 1938.

This rare anomaly was seen in a child 1 year of age. The child did not follow light. There was no nystagmus. The anterior portions of the eye were normal. The pupils were inactive to light but varied in size from time to time, irrespective of stimulus. The media were clear. The fundus reflex was pale red. In place of the optic nerve head there was a deep excavation, the floor of which was about 5 diopters beyond the level of the fundus. Its color was gray. From the floor of the pit emerged only minute threads, representing retinal vessels, the lower branch in the right eye being the only one which contained more than a trace of blood, and even this appeared to fade out soon after leaving the edge of the excavation.

The article is illustrated.

W. Zentmayer.

General Diseases

BERIBERIC RETROBULBAR NEURITIS. F. J. SORIANO and M. I. PUIGGARI, Arch. de oftal. de Buenos Aires **13:** 244 (May) 1938.

After reference to the ocular symptoms connected with avitaminosis A, C and D, the authors consider avitaminosis B. They discuss at considerable length the production of this type of avitaminosis, observed mostly in persons eating shelled rice.

Avitaminosis B attacks the motor, sensory and optic nerves, and appears in two forms: (1) a dry, or paralytic, form, with marked muscular atrophy and some anesthesia, and (2) an edematous, or dropsical, form, with generalized edema and violent pain.

The manifestations due to involvement of the ocular nerves are numerous and frequent, and all the ocular nerves may be involved. The optic nerve is frequently affected; according to Japanese writers, it is usually affected. Involvement of this nerve appears as retrobulbar neuritis with a central scotoma and atrophy of the papillomacular bundle. The scotoma is characterized by a scotomatous bridge joining the scotoma proper with the blindspot.

The author reports a case in which retrobulbar neuritis was the sole symptom of beriberi.

A woman who had suffered great privations in Spain, having subsisted for some time on an almost exclusive diet of rice, with no meat, fat or milk, suffered from loss of sight and loss of 20 kilograms of weight. There was a central scotoma of the type described. The use of alcohol and tobacco could be excluded as well as the use of hair dyes. There was no diabetes, and the blood and urine were normal.

The authors consider the prognosis poor as regards a permanent improvement of vision, as they believe the lesion to be stationary.

C. E. FINLAY.

Glaucoma

CYCLODIALYSCLERECTOMY: ANTIGLAUCOMATOUS OPERATIONS. E. GORNET, Ann. d'ocul. **175:** 678 (Sept.) 1938.

As the title implies, this operation consists in uniting sclerectomy and cyclodialysis into one operation. It is not a question of denying the good effect of a limbic sclerectomy or of cyclodialysis but a question of attempting to correct the failures of one or the other operation in the association of the two.

The author describes the two operations minutely.

A bibliography accompanies the article.

S. H. MCKEE.

TREATMENT OF ABSOLUTE PAINFUL GLAUCOMA BY ROENTGEN THERAPY. P. SATANOWSKY, Arch. de oftal. de Buenos Aires **13:** 227 (May) 1938.

After reference to, and a comparison of, various methods of treatment recommended for the relief of the intolerable pain in cases of

absolute glaucoma, such as opticociliary neurotomy, enucleation and retrobulbar injections of alcohol, the author reports 3 cases in which relief was obtained by roentgen therapy, a procedure first employed by Hessberg in 1920.

The literature on the subject is reviewed. C. E. FINLAY.

Injuries

KERATOCONJUNCTIVITIS FROM CHESTNUT BURS. C. DEJEAN and R. GUIGNOT, Arch. Soc. d. sc. méd. et biol. de Montpellier **19:** 70, 1938.

A dried chestnut shell on hitting a child's eye produced an irritation for over two months, with photophobia, lacrimation, diminished visual acuity, edema of the lids, chemosis and mucopurulent secretion. The slit lamp revealed from seven to eight punctiform leukomas of rusty color, probably representing the spicules of the chestnut bur. Fortunately the débris was eliminated spontaneously, with considerable visual recovery.

J. E. LEBENSOHN.

TWO STAGE ROENTGEN OBSERVATION DURING OPERATION FOR INTRAOCULAR FOREIGN BODIES: REPORT OF CASES. R. TERTSCH, Klin. Monatsbl. f. Augenh. **100:** 339 (March) 1938.

Tertsch describes a new method for removing foreign bodies of weak magnetic or nonmagnetic power from the eyeball. His method is based on the principles reported by George H. Cross in 1927. Tertsch refers to the excellent work done in this realm by von Szily during the World War. The method, described in detail, centers in the use of two roentgen spheres in connection with a superastral screen. Two tubes are fitted to the spheres so as to limit irradiation to a circular opening with a diameter of 30 mm. The tubes contain a filter which allows illumination for several minutes without injuring the skin. The two superastral screens, with a surface of about 5 sq. cm., are fastened to a handle. An appliance is being prepared which will permit fastening the screen to the patient's head. The two bundles of roentgen rays unite in the region of the foreign body at an angle of approximately 90 degrees in a manner which will furnish two pictures situated perpendicularly to one another. Interchanging observation of the two pictures allows orientation and depth vision, enabling the operator to approach the foreign body readily with his instrument. Lesion of the healthy eye is rendered impossible by proper devices. The roentgen spheres are focused by pedals worked with the foot. The room is darkened, and the operator wears a head light sufficient to illuminate the operative field. Its weak light does not interfere with the luminescence of the roentgen pictures. A detailed description of the instruments is given, and the use of the method is illustrated by 3 cases in which operation was successful.

K. L. STOLL.

Lacrimal Apparatus

LACRIMAL LAMINARIA IN THE SURGICAL THERAPY OF ATRESIA OF THE NASAL CANAL. P. ZARZYCKI, Bull. Soc. d'opht. de Paris **50:** 306 (June) 1938.

In gynecology Laminaria (seatangle) renders a great service. In ophthalmology, because of blunders of technic, it has been neglected. It is superior to metal sounds, which cause trauma to live tissue and necessitate frequent treatments. It is more rigid than the fiber sound and has the advantage of increasing its bulk slowly over a period of hours. Its use is contraindicated in cases of osteitis, tuberculosis or syphilis affecting the region of the lacrimal sac, obstruction due to foreign body, exostoses and polyps. Zarzycki outlines the technic for the use of seatangle. The details given are too numerous and lengthy to be recorded here.

L. L. MAYER.

Lens

HEREDITARY DEGENERATION OF THE RAT RETINA (ASSOCIATED WITH CATARACT). M. C. BOURNE, D. ADAMS CAMPBELL and KATHARINE TANSLEY, Brit. J. Ophth. **22:** 613 (Oct.) 1938.

This paper deals with a study of the retina of rats with hereditary cataractous lenses. Briefly, the changes in the retina were of the nature of progressive degeneration beginning with the death of the rod nuclei. The subsequent alteration in the structure of the retina leading ultimately to disintegration of the inner nuclear and ganglion cell layers appears to be the result of the disappearance of the neuroepithelium. There were no gross vascular changes in the retina, and the blood vessels of the choroid remained unaffected until an advanced stage of retinal degeneration. The authors were impressed by the striking resemblance which the histologic picture of this lesion in certain stages of development bears to the microscopic appearance described in certain cases of retinitis pigmentosa.

The article contains a number of illustrations.

W. ZENTMAYER.

Lids

THE GENESIS OF EPITARSUS. G. ANASTASI, Ann. di ottal. e clin. ocul. **66:** 202 (March) 1938.

A man, aged 22, showed symmetric folds of conjunctiva near the upper border of both upper tarsi. A probe could be passed upward beneath each fold into the retrotarsal folds. The conjunctiva and eyes were otherwise normal. Purulent conjunctivitis had been present in both eyes at birth, and the author believes that the condition was caused by applications of the silver nitrate stick. It was, therefore, simply a peculiar form of symblepharon and not a congenital anomaly.

A bibliography accompanies the article.

S. R. GIFFORD.

Neurology

OCULAR ORIGIN OF MIGRAINE IN CHILDREN AND YOUNG PERSONS. K. GRUNERT, München. med. Wchnschr. 85: 1337 (Sept. 2) 1938.

For ten years Grunert made careful functional tests on the eyes of all patients who were subject to headaches and to migraine and, as far as possible, of the relatives of these patients. In the course of these studies he made two significant observations:

1. In the majority of the patients with headaches and in nearly all of those with migraine there existed disturbances in the ocular function.

2. The treatment of these ocular disturbances reduced or completely removed the general symptoms to such an extent that a causal connection could not be denied. In children and young persons the ocular origin of migraine was even more pronounced than it was in adults.

The author reports observations on more than 200 children and young persons with migraine. Many of the children were of the type referred to as "difficult"; that is, they showed signs of nervous irritability, were difficult to manage or were inattentive in school. Ocular examination disclosed defective refraction, disturbances in the ocular equilibrium and defects in accommodation. In many of these children the growth of the eyes is not completed as early as in others, and school, which requires a considerable amount of close work, involves a great strain on these still growing eyes. After describing some of the difficulties of these children and of the symptoms likely to develop in them, the author directs his attention to the treatment of migraine of ocular origin. He emphasizes that even slight optic defects may cause severe subjective disturbances. After the refractive defects have been corrected, close work is avoided for one or two weeks, and the weakened muscle of accommodation is treated with pilocarpine. The administration of pilocarpine must be individualized. It is best to administer it in the evening before the patient goes to sleep. In cases of severe defects it can be given also during the day, but the individual doses are, of course, smaller. In cases of disturbances in the muscular equilibrium or in latent strabismus prisms are employed; occasionally an operation for strabismus may be resorted to, or stereoscopic exercises may be employed. In the few cases in which no anomalies of refraction exist and in which there is no impairment of the muscular equilibrium but only an insufficiency of the apparatus of accommodation, the migraine is cured by resting the eyes for a while and by treatment with pilocarpine. The ocular treatment effected cure in 197 children and young persons with migraine. The author closes his report by recommending that all children in whom migraine is suspected be subjected to a thorough examination of the eyes.

J. A. M. A.

Ocular Muscles

RELATIONSHIP OF HETEROPHORIA TO DIVERGENCE AND CONVERGENCE, BASED ON CLINICAL MEASUREMENTS. F. H. HAESSLER, Am. J. Ophth. 21: 272 (March) 1938.

Haessler discusses heterophoria and after extensive tests gives the following summary and conclusion:

"In 1,000 patients who came for refraction, it was shown that the degree of exophoria or esophoria was not determined by a balance between divergence and convergence as expressed in the usual clinical measurements."

W. S. REESE.

OPERATION IN A CASE OF MARCUS GUNN PHENOMENON. A. and G. OFFRET, Bull. Soc. d'opht. de Paris **50:** 61 (Feb.) 1938.

The family of a girl of 9 years insisted that an operation be done for ptsois of the right eyelid. The eyelid covered a greater part of the cornea and was accompanied by a limitation of elevation of the globe. In mastication, when the mouth opened the lid raised, only to return to the original position when the mouth was closed. The operation used has been described by Nida (*Ann. d'ocul.* **166:** 639, 1929). It consists of an insertion of the tendon of the superior rectus muscle into the tarsus of the upper lid. Two and one-half years after operation the child's lid still remained motionless when the mouth was opened. There was also no movement of the lid on mastication. A bibliography accompanies the article.

L. L. MAYER.

Orbit, Eyeball and Accessory Sinuses

LUXATION OF THE EYEBALL INTO THE ANTRUM; ILLUSIVE ANOPHTHALMOS DURING AUTOPSY: REPORT OF A CASE. A. JESS, Klin. Monatsbl. f. Augenh. **100:** 353 (March) 1938.

After a brief review of the literature in point, the author reports the case of a woman, aged 64, who injured her eye by falling against the edge of a door. The conjunctiva was retracted funnel shape; blood oozed from the orbit, and a cloud was observed in the right antrum on roentgen examination. Operation revealed remnants of vitreous, sclera and finally the collapsed eyeball, which was removed with a stump of the optic nerve measuring 1 cm. After removal of a large blood clot from the antrum, the wound healed promptly. The eyeball had slipped into the antrum through a fracture of the floor of the orbit. In another case, reported to Jess, a soldier died from a fractured skull after falling off a roof. No eyeball was observed in one orbit during autopsy, so that the question arose as to whether the man wore a prosthesis and escaped detection during his military services. Although his wife persisted in stating that he had two good eyes, proof was lacking, as the body had been buried. Altercation with insurance companies are discussed in this respect. The cases referred to include 1 reported by Becker, that of a farmer girl who suffered subluxation of the eyeball into the antrum by the thrust of a cow's horn, and the case of the boy who could see through one nostril after a similar injury, which occurred in 1575. Both accidents happened in Heidelberg.

K. L. STOLL.

Pharmacology

HUMAN AUTONOMIC PHARMACOLOGY: XI. EFFECT OF BENZEDRINE SULFATE ON THE ARGYLL ROBERTSON PUPIL. ABRAHAM MYERSON and WILLIAM THAU, Arch. Neurol. & Psychiat. **39:** 780 (April) 1938.

"The complete Argyll Robertson pupil is one in which the pupil is miotic to the extreme point and there is no reaction to darkness, flash-light or daylight, while the reaction in accommodation is preserved. In our opinion [the authors'], other reflexes are not clinically essential.

"The incomplete Argyll Robertson pupil is one in which there is some dilatation of the pupil. This pupil does not react to flash-light but will widen slowly in the darkness and constrict slowly in a room well illuminated by daylight.

"The light reflex may be restored in a partial way in the Argyll Robertson pupil by instillation of a dilute solution of benzedrine sulfate, ranging from 0.125 to 0.5 per cent, or by repeated subcutaneous injection or oral ingestion of the drug. Under such circumstances the pupil dilates, and while ordinarily only slightly mobile to flash-light, it widens in darkness and constricts in daylight, the movements of dilatation and constriction being slow and deliberate but certain.

"The light reflex, so far as the pupil is concerned, must be considered as made up of two important parts: (1) dilatation of the pupil to darkness or to partial illumination and (2) constriction to light, these movements being brought about by the reciprocal activities of the sympathetic and the parasympathetic nervous system, or, to speak chemically, by a balance between adrenergic and cholinergic substances. Furthermore, part of the light reflex is widening and narrowing of the palpebral fissure, widening taking place in darkness or in lessened illumination and constriction under the influence of light or increased illumination."

R. IRVINE.

Physiologic Optics

CLINICAL RESEARCHES ON THE DIOPTRIC POWER OF THE HUMAN LENS. R. CAMPOS, Ann. di ottal. e clin. ocul. **66:** 413 (June) 1938.

After a technical consideration of various means of estimating the refractive power of the lens, Campos concludes that the only method at one's disposal is that of studying the change in refraction after removing the lens. On the basis of 15 cases in which the formula of Bierke, as modified by Gullstrand, was employed, Campos found the dioptric power of the lens to vary between 19 and 26 diopters, with an average of 22 diopters.

S. R. GIFFORD.

Physiology

AUTONOMIC INNERVATION OF THE FACE: II. AN EXPERIMENTAL STUDY. F. H. LEWY, ROBERT A. GROFF and F. C. GRANT, Arch. Neurol. & Psychiat. **39:** 1238 (June) 1938.

In a previous paper the author demonstrated that after section of the oculomotor nerve electrical stimulation of the first division of the fifth nerve is followed by widening of the ipsilateral palpebral fissure

and lacrimation. The muscular contraction was slow and was sustained for a period after electrical stimulation was stopped.

The present work elaborates on this phenomena, showing that the pseudomotor phenomena of the eyelid, the lip, the whiskers and the tongue may be elicited by stimulation of: (1) autonomic efferent fibers in the sensory root or sensory divisions of the fifth nerve originating in the mesencephalic nucleus of the nerve and (2) the preganglionic and postganglionic fibers of the cervical portion of the sympathetic trunk.

They conclude that in the sensory root of the fifth nerve as well as of the third, seventh and twelfth nerves, respectively, efferent fibers pass from the mesencephalic nucleus to the face.

This article should be interesting to ophthalmologists as a suggestion toward the explanation of such bizarre oculomotor phenomena as jaw-winking and the pseudo-Graefe phenomena.

R. IRVINE.

BEHAVIOR OF THE OCULAR TENSION OF NORMAL PERSONS UNDER ATMOSPHERIC DECOMPRESSION. A. BUCALOSSI, Ann. di ottal. e clin. ocul. **66:** 292 (April) 1938.

The author examined 12 normal persons from 18 to 24 years of age in a pressure chamber. Pressure was reduced to 490 mm. of mercury at a rate of 13.5 mm. per minute and maintained at the lowest point for fifteen minutes. A slight increase of tension (from 2 to 4 mm. Schiötz) was seen in most of the subjects at the time of minimum pressure. This was parallel with a similar rise of blood pressure and returned to normal when the atmospheric pressure became normal.

S. R. GIFFORD.

STUDIES ON DARK ADAPTATION WITH AUTOMATIC RECORDING OF THE THRESHOLD VALUES. W. KYRIELEIS, Arch. f. Ophth. **138:** 564 (May) 1938.

In 1936 Kyrieleis demonstrated before the German Ophthalmological Society at Heidelberg an attachment to the Engelking-Hartung adaptometer which records on a kymograph the width of the Aubert diaphragm of the adaptometer. With this adaptometer the light thresholds are determined by opening the Aubert diaphragm until the patient sees light. A record of the widths of the diaphragm at these threshold points is, therefore, a record of the respective light sensitivities. With this method it is possible to make ten or more threshold determinations per minute. Dark adaptation curves obtained in this way show a few heretofore unknown details. In the rise of the light sensitivity of the retina during dark adaptation a fairly regular alternation of periods of rapid and slow rise can be observed. The adaptation curve thus appears to consist of numerous short arcs or to describe small steps. The author has studied in detail the effect of exposure to varying degrees of light immediately before dark adaptation and the effect of variations in the size of the pupil. The position of the nick in the adaptation curve is characteristically dependent on the degree of light adaptation prevailing immediately before dark adaptation.

P. C. KRONFELD.

Refraction and Accommodation

STUDIES ON THE HEREDITARY ORIGIN OF MYOPIA. L. PAUL, Arch. f. Ophth. **139:** 378 (Sept.) 1938.

The relationship between the refraction of parents and the refraction of their children is studied statistically in material comprising about 4,000 Germans. The results are shown in the accompanying table.

The clinician distinguishes between low degrees of myopia without any tendency toward chorioretinal complications and high degrees of myopia (myopia gravis) characterized by a definite tendency toward such complication. Paul sets the borderline between the two degrees at a myopia of 10 diopters and finds that the two degrees are transmitted separately and independently of one another. In other words, myopia gravis occurs much more frequently in families in which one parent is affected with myopia gravis than in families in which one parent is affected with a low grade of myopia. On the other hand, myopia of low degree is relatively rare in families in which one parent is affected with myopia gravis.

Statistical Study of Myopia

	A No. of Families Examined	B No. of Children in These Families	C No. of Children Examined	No. of Myopic Children, Expressed in % of B	No. of Myopic Children, Expressed in % of C
No parent myopic	423	1,173	723	7.85	12.72
One parent myopic	166	479	297	23.00	37.10
Both parents myopic	39	98	72	53.10	72.20

The frequency of myopia of low degree is greater in female than in male infants. During the period of growth this relationship changes, so that (in families with myopia in the ancestry) myopia is more frequent among men than among women. Here the author admits the possibility of the development of myopia through the influence of extrinsic factors. These factors, however, are supposed to be especially effective in persons with myopia in their ancestry.

P. C. KRONFELD.

Retina and Optic Nerve

THE CLINICAL SIGNIFICANCE OF THE RETINAL CHANGES IN THE HYPERTENSIVE TOXEMIAS OF PREGNANCY. G. G. GIBSON, Am. J. Ophth. **21:** 22 (Jan.) 1938.

Gibson gives the following summary of his study of the retinal changes in 39 cases in which a diagnosis of toxemia of pregnancy or of varying degrees of preeclampsia was made:

"The first visible physical sign of early preeclampsia is attenuation of the nasal retinal arterioles. This is usually concurrent with slight elevation of the diastolic blood pressure. The great majority of these cases do not become sufficiently severe to progress further than this stage; they will usually respond to medical treatment as suggested by

Arnold. If they do, the patient will be left without a demonstrable vascular lesion. In a small percentage of the cases, however, the disease is much more fulminating and treatment must be heroic. The earliest and most reliable signs of the severe course of these conditions is the appearance of the retinal arterioles. The severe changes in the retinal arterioles usually precede the clinical criterion of severity in these conditions. The appearance of hemorrhages and exudates associated with hypertensive vascular change in the retinal arterioles is a reliable sign for the therapeutic termination of pregnancy. Proper interpretation of these changes will materially reduce the vascular damage done to the mother, and reduce the incidence of fetal and maternal mortality."

W. S. REESE.

CONTRIBUTION TO THE STUDY OF THE GENESIS OF DETACHMENT OF THE RETINA. E. REDSLOB, Ann. d'ocul. **175:** 637 (Sept.) 1938.

The vogue for studies on detachment of the retina seems to have abated somewhat. In the last ten years more than 600 articles on this subject have appeared. Have they cleared up all the questions connected with this subject? It seems to the author that though a satisfactory therapeutic technic may have been arrived at, the question of origin is still much to the fore.

The important role attributed to the closing of the tear is known to all ophthalmologists, but in a consideration of whether the tear is the principal etiologic factor in the development of the detachment, different opinions are encountered. Unquestionably there are cases of detachment in which despite the most minute examination with the ophthalmoscope and microscope no sign of a tear is to be found. Such a case of relatively fresh detachment, in which histologic examination eliminated all possibility of perforation of the retina, was reported by the author a few years ago. One may conclude that the mechanism in the development of detachment of the retina is still imperfectly known, and it seems useful to bring together all possible facts in order to arrive at a better understanding of the problem.

The author gives in detail the results of histologic examination of an enucleated globe with two illustrations.

S. H. MCKEE.

OXYCEPHALY AND ALTERATIONS OF THE OPTIC NERVE. G. P. SOURDILLE and M. DAVID, Bull. Soc. d'opht. de Paris **50:** 206 (May) 1938.

A boy of 7 had had poor vision for one and one-half years, and for the past six months his sight had been rapidly diminishing. When aged 3 months the child had a severe enteritis with abnormally late closure of the fontanels. His head was of the typical tower skull variety. Normal intelligence but an emotional instability were noted. The visual acuity of the right eye was 2/10 and that of the left eye was 1/12, with correction by a horizontal convex cylinder to 3.5/10 and 1/10, respectively. There was concentric contraction of the visual fields, more marked on the left, to about 40 degrees. The right disk was completely pale, and the left showed pallor only in the temporal region. Roentgenograms of the skull showed the two characteristics of oxycephaly, namely, digital

markings of the convexity, here most formidable, and enlargement of the middle fossa. It is the authors' belief that in this case the atrophy was due to intracranial hypertension. Decompression resulted in vision of 4/10 for the right eye, while the left remained at 1/10 after six weeks. The question of operation in these cases is open for discussion.

L. L. MAYER.

CALCIUM-POTASSIUM VALUES OF THE BLOOD IN RETINAL DETACHMENT. A. BUCALOSSI, Ann. di ottal. e clin. ocul. **66:** 371 (May) 1938.

Previous studies by the author had shown a diminution in the alkaline reserve of patients with retinal detachment. Since potassium is known to favor imbibition of the proteins while calcium inhibits it, possible effects of one or the other ion on the condition of the vitreous are considered. In 10 normal persons the author found an average potassium value of 20.34 mg. per hundred cubic centimeters of blood and a calcium value of 16.44 mg., giving a potassium-calcium quotient of 1.96. The maximum quotient was 2.34 and the minimum 1.60. In 24 patients with idiopathic retinal detachment the average potassium value was 19.11 mg. per hundred cubic centimeters and the average calcium value, 11.14 mg., giving a quotient of 1.71. In 25 per cent of patients the quotient was lower than the lowest of the normal series, while in 75 per cent it was lower than the average of this series. There was no correlation between the potassium-calcium quotient and the alkaline reserve. The increase in calcium might conceivably be a factor in changing the physiochemical constitution of the vitreous in the sense of decreased imbibition of its proteins.

S. R. GIFFORD.

BILATERAL AMAUROSIS DUE TO ANATOMIC AND FUNCTIONAL CHANGES IN THE RETINAL CIRCULATION. C. GANDOLFI, Rassegna ital. d'ottal. **7:** 287 (May-June) 1938.

The author reports 2 cases of closure of both central retinal arteries in which careful observation of the condition of the retinal vessels, including determinations with the dynamometer, revealed a different basis for the condition in each case. One case was that of a man of 73 who had suddenly lost vision in each eye two days previously. When he was first seen the vessels were normal in appearance, but vision improved only slightly in spite of repeated injections of acetylcholine. The general blood pressure dropped markedly after the first injection, and the retinal blood pressure became normal. The author considers that the condition was due to spasm of the retinal arteries. In the second case loss of vision in one eye was followed within a day by the occurrence of the same condition in the second eye. The usual fundus picture of closure of the retinal arteries was present in each eye with other signs of arteriosclerosis. Because of these other changes and because the retinal blood pressure remained unvaried at a low level, the condition in this case was interpreted as organic closure of both central arteries, due in all probability to endarteritis and thrombosis. Retrobulbar injections of acetylcholine were of no effect.

S. R. GIFFORD.

Trachoma

PATHOLOGIC ANATOMY OF THE TRACHOMA FOLLICLE. G. BORSELLO, Rassegna ital. d'ottal. **7**: 361 (May-June) 1938.

The literature on the pathologic anatomy of the trachoma follicle is reviewed, and the author reports his studies of material stained by various methods, including the silver stains and the stains of Giemsa and of Pappenheim. The article is 45 pages in length and does not lend itself to abstracting.

Photomicrographs and a bibliography are included.

S. R. GIFFORD.

ATTEMPTED CULTURE OF THE TRACHOMA AND PARATRACHOMA VIRUS. I. JOHN and F. A. HAMBURGER, Arch. f. Ophth. **138**: 760 (July) 1938.

"Almost exclusively" material (pieces of conjunctiva) from patients with paratrachoma (apparently chiefly cases of inclusion blennorrhea of the newborn) were used for culture experiments, the results of which were disappointing on the whole. Purification of the material, that is, removal of all bacteria, was first done by filtration which entailed dilution of the virus, so that inoculation of baboons with the filtrate had no effect. These filtrates must have contained the virus, because by centrifuging the filtrate at high speed and incubating its sediment together with human embryonic tissue for a few days a material was obtained which microscopically contained bodies similar to the elementary bodies and produced a paratrachoma-like conjunctivitis in the baboon. In various culture mediums which were inoculated with paratrachoma material no Prowazek-Halberstädter inclusions or initial bodies developed, but structures which resembled elementary bodies more or less closely were seen occasionally. Unfortunately, there is no truly specific staining method for elementary bodies. Aside from the intrinsic difficulties of this kind of work, the authors were handicapped by scantiness of clinical material and of experimental animals (baboons).

P. C. KRONFELD.

Tumors

ANNUAL REPORT OF RADIUM INSTITUTE FOR 1937, editorial, Brit. M. J. **2**: 712 (Oct. 1) 1938.

Twenty-eight cases of tumors of the limbus were reported, most of the growths being squamous cell epitheliomas. These were treated by unscreened radium plaques placed in contact with the growth, and no instance of cataract was recorded. In all but 2 cases, in which enucleation was subsequently performed, the results were completely satisfactory.

It is hoped that the patients will be kept under careful observation, so that any possible subsequent effects of irradiation on the retina will be recorded.

ARNOLD KNAPP.

LEUKOSARCOMA OF THE CHOROID: REPORT OF A CASE. G. MATHIS, Rassegna ital. d'ottal. **7:** 408 (May-June) 1938.

A patient of 71 had been losing vision in one eye for four years, with recent attacks of pain and hypertension. A gray mass protruded into the anterior chamber through the root of the iris. At enucleation, extension of the neoplasm through the sclera was seen. No pigment was found in the tumor, which was of the mixed cell alveolar type. The intraocular portion was relatively small compared to the orbital extension and was of the flat type.

S. R. GIFFORD.

Uvea

TUBERCULOSIS, SYPHILIS AND CHRONIC ANTERIOR UVEITIS. F. FARINA, Rassegna ital. d'ottal. **7:** 301 (May-June) 1938.

Aside from the typical forms of uveitis, which may be rather definitely diagnosed as due to syphilis, tuberculosis or focal infection, the author has interested himself especially in a group of cases in which the uveitis is of the type usually ascribed to various other causes, such as gout, rheumatism, diabetes and intestinal infections. In such cases the uveitis responds poorly to treatment and is prone to recurrence. Farina reports 40 such cases seen during nine years, the patients having been followed from three to five years. In addition to complete physical examination, including serologic tests, tuberculin tests and an analysis of the blood chemistry, he has in many cases examined the aqueous microscopically and considers his observations of considerable value. The presence of lymphocytes and a large number of crystals is considered evidence in favor of a tuberculous origin. In cases in which the uveitis is due to syphilis, polymorphonuclear leukocytes and pigment granules are found in larger numbers, with fewer crystals. Two cases are reported in which the diagnosis of syphilis was made on this basis and the Wassermann reaction, previously negative, became positive after antisyphilitic treatment. The patients had no recurrences during further observation. In another case a diagnosis of tuberculosis was made chiefly because of changes in the aqueous, and the administration of tuberculin resulted in apparent cure. Although only 4 cases are reported in detail, the author states that similar events occurred in many of the other cases, the serologic tests or the cutaneous tests becoming positive during treatment.

S. R. GIFFORD.

Society Transactions

EDITED BY W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

ALEXANDER G. FEWELL, M.D., *Chairman*

Dec. 15, 1938

WARREN S. REESE, M.D., *Clerk*

IRIDESCENT CRYSTALS IN THE CRYSTALLINE LENS. DR. ALEXANDER G. FEWELL and DR. STIRLING S. MCNAIR.

The literature has been reviewed with special reference to cases in which the crystalline lens contained iridescent crystals. The presence of ordinary crystals in the lens is not uncommon, but the occurrence of iridescent crystals is indeed rare. In most of the reported cases of iridescent crystals in the lens the crystals contained some calcium salt, protein or one of the amino acids. In our search through the literature we are able to find only 1 case, that reported by Beresinskaja, in which chemical analysis proved cholesterol crystals to be present. In a majority of the cases reported the iridescent crystals were found bilaterally. Although these crystals are supposedly due to degenerative changes in a cataract, the majority of the case reports state that the remaining portion of the lens is clear. It is surprising how few lenses containing iridescent crystals have been extracted and examined chemically.

The case reported here is that of a Negress aged 69 who had bilateral anterior polar cataract in addition to bilateral senile cataract. She had had diabetes for the past four years and also suffered from hypertension. The vision in the right eye was 3/60 and in the left eye 2/60. Examination of the right eye with the slit lamp revealed large masses of brownish golden glistening crystals, somewhat tightly packed together in places, more dense and numerous in the center and on the temporal side. These crystals were mostly in the stroma of the lens, and the remainder of the lens was relatively clear. The fundus was seen with difficulty on account of these crystals and the opacities of the lens. The disk was somewhat dusky, the arteries were reduced in caliber and some retinal changes were seen in the macular area but no hemorrhages. The left eye showed a mature cataract but no crystals. The fundus could not be seen. We expect to extract the lens of the right eye and subject its crystals to microchemical examination. We hope to report the results of this examination at a later date.

DISCUSSION

DR. ALFRED COWAN: The case which I reported here three or four months ago was different from this one. In my case the crystals were brightly colored—red, green, yellow and orange—and were more or less

densely arranged in a zone in and around the adult nucleus. Actually, presenile, zonular cataract which had undergone degeneration was present. I would consider the condition in the case reported an atypical complicated cataract.

DR. WILLIAM ZENTMAYER: Some years ago Dr. Verhoeff reported a case of coralliform cataract in which a thorough analysis of the crystals of which the opacity was formed showed them to be protein. Soon after this report I removed a lens with the same type of cataract and sent it to Dr. Verhoeff. The analysis showed the same type of crystals as was found in his own case.

ESSENTIAL SHRINKING OF THE CONJUNCTIVA (OCULAR PEMPHIGUS): PEMPHIGUS OF THE MUCOUS MEMBRANES. DR. JOSEPH V. KLAUDER and DR. VAN M. ELLIS.

R. H., a white youth aged 21, was unable to state exactly when the present condition started, but he had had ocular trouble at the age of 4 years. At this age he was said to have had a growth on the right eye. When he was examined at the age of 21 the right cornea was clear. There was adhesion of the conjunctiva of the lower lid to the bulbar conjunctiva, obliterating the cul-de-sac. The upper cul-de-sac was narrowed; there was no adhesion of the conjunctiva of the upper lid to the bulbar conjunctiva. The left cornea also was clear, and there was no involvement of the conjunctiva. The cul-de-sacs were, however, narrowed. The vision was unimpaired. There was no involvement of the mucous membranes of the nose, mouth, throat, urethra or anus. There had never been any cutaneous involvement.

OLD INTERSTITIAL KERATITIS. DR. JOSEPH V. KLAUDER and DR. VAN M. ELLIS.

A white man, aged 58, came to the clinic because of poor vision. He had always had poor vision and had worn glasses for many years. He was an only child. He remembered having sore eyes when a child but could not recall any details. He said that he had never had a genital lesion. After a "blood" test ten years previously he had received injections in the arm at intervals for three months.

The pupils were unequal and irregular in outline. The right pupil was fixed to light, and the left reacted slightly. Gross inspection of the corneas showed faint opacities. The vision with correction was 6/15 in the right eye and 6/30 in the left eye. Slit lamp examination of the right eye revealed the central portion of the cornea to be gray with a moderate loss of smoothness. The posterior surface was thickened and fairly opaque and contained a number of old blood vessels, deeply situated. Examination of the left eye gave essentially the same results. The patellar reflexes were absent, and the Romberg sign was positive. The patient presented no stigmas of congenital syphilis, except very suggestive facies, and he had no subjective symptoms of tabes. The Wassermann reaction of the blood was 4 plus; the Meinicke reaction was 2 plus. Examination of the spinal fluid gave negative results in all phases.

This case is reported to call attention to the importance of being conscious of the cornea in examining patients of any age suspected or

known to have syphilis. This applies more to the clinician and the syphilologist than to the ophthalmologist, who is more cognizant of the significance of old corneal opacity as a clue in the diagnosis of old interstitial keratitis than is any other specialist.

Corneal examination, especially slit lamp microscopy, may be an important procedure in examination of a patient, especially an adult with a positive Wassermann reaction. These examinations may be the only means of determining that the patient has congenital syphilis.

EFFECTIVE TREATMENT OF LUPUS ERYTHEMATOSUS AND EXUDATIVE RETINITIS WITH A GOLD COMPOUND. DR. JOSEPH V. KLAUDER and DR. VAN M. ELLIS.

E. D., a white man aged 36, was first seen in April 1938, at which time he exhibited on each side of the face and on the forehead bright red areas ranging in size from that of a dime to that of a half dollar. Some of the areas were infiltrated, and all were devoid of scales. The scalp and mucous membranes were not involved. Ophthalmoscopic examination revealed various-sized, irregular, fluffy, cloudlike patches scattered throughout the fundus of the right eye, particularly around the disk. There were three small fresh hemorrhages around the macula. The appearance of the left eye was the same as that of the right eye, but the involvement was not so extensive. Vision was 3/60 in each eye. Three months prior to the time he was first seen the patient had chills, fever, general malaise, weakness and tiredness, which necessitated rest in bed. About that time an eruption developed on the face. A month later he noticed blurring of vision. He was incapacitated from January 1938 until about April because of progressive weakness and loss of 23 pounds (10.4 Kg.) in weight. There was no history of tuberculosis; the patient had always been underweight but of good general health. The Mantoux reaction to a 1:100 dilution of tuberculin was negative. Roentgenograms of the lungs were negative, as were the results of examination of the sputum for tubercle bacilli. Urinalysis gave negative results, and the Wassermann reaction of the blood was negative. The blood sugar content was 71.7 mg. per hundred cubic centimeters; the urea, 13.6 mg., and the uric acid, 3.1 mg. A complete blood count on March 26 showed: red blood cells, 4,640,000; white blood cells, 3,400; polymorphonuclears, 46 per cent; eosinophils, 1 per cent; lymphocytes, 45 per cent, and monocytes, 8 per cent. On April 1 the white blood cells numbered 6,200 and on April 4, 8,300. Histologic examination showed subacute diffuse dermatitis and atrophy of the epidermis with local hyperplasia.

Beginning April 1938, the patient was treated with gold and sodium thiosulfate intravenously (the maximum dose, 50 mg.) and bismuth salicylate (2.5 cc.) intramuscularly. These drugs were given in courses at weekly intervals. Apparently the treatment was effective. The cutaneous lesions disappeared, and the patient gained 15 pounds (6.8 Kg.) in weight and is no longer tired. The appearance of the fundi improved. At present the retinitis is quiescent. The optic disk has a pale white tint and is well outlined. Some of the larger vessels have been replaced by scar tissue; other vessels are sclerosed and have a corkscrew appearance. The vision in each eye is 6/60. Collateral circulation was observed over each disk.

DISCUSSION

DR. WALTER I. LILLIE: In regard to the case of lupus erythematosus, examination of the fundi revealed a diffuse perivasculitis and periphlebitis associated with pallor of the disks and the formation of new blood vessels around and involving each disk. Although a retinitis specific for lupus erythematosus has never been described, the retinitis observed before the therapy with gold and sodium thiosulfate was instituted could have been of toxic origin.

The present change in the fundi is similar to that which occurs after the intravenous administration of quinine in a person with an idiosyncrasy to quinine.

In my experience, gold and sodium thiosulfate has produced no untoward ocular effects and has been efficacious in the treatment of posterior uveal disease.

DR. H. MAXWELL LANGDON: I should like to ask Dr. Klauder whether he thinks there have been any progressive changes in the case of pemphigus since he first saw the patient. Frankly, the condition does not look like pemphigus to me. I have never seen pemphigus limited to the lower cul-de-sac and have never seen it last so long without the other eye becoming involved. On the basis of a history of ocular trouble at 4 years of age, it looks to me as though the condition might be scarring due to the inflammation seventeen years ago rather than pemphigus.

Concerning the patient with interstitial keratitis, has Dr. Klauder thought of the possibility of acquired syphilis? I admit that the likelihood is slight, but such cases do occur.

DR. JOSEPH V. KLAUDER: We are glad to know Dr. Langdon's opinion regarding the case of suspected pemphigus. We are inclined to regard the condition as progressive. It appears to be more pronounced now than at the time we first saw the patient. In formulating our opinion of ocular pemphigus in this patient, we were not entirely influenced by the presence of symblepharon. We placed considerable significance on the dry, lusterless, wrinkled appearance of the bulbar conjunctiva external to the cornea and above the symblepharon. The appearance was that of shrinking, and it is a conspicuous symptom eventually in all patients with ocular pemphigus. However, we will keep the diagnosis open pending further observation.

Regarding the cases of interstitial keratitis, I have never observed interstitial keratitis in a patient with acquired syphilis. Igersheimer has stated that when syphilis is acquired in infancy or childhood interstitial keratitis is likely to appear in adult life. Other authors have expressed the belief that when chancre involves the conjunctiva interstitial keratitis is likely to appear subsequently. In many of the reported cases of interstitial keratitis occurring in association with acquired syphilis that I have reviewed, I did not regard the evidence sufficient to prove that syphilis was acquired. For example, a history of a genital lesion is no proof that that lesion was a chancre. In still other reports there was no slit lamp evidence to support the diagnosis of interstitial keratitis.

PRODUCTION OF CORNEAL ULCERS IN THE RABBIT. DR. ROBB MCDONALD and DR. HORACE PETTIT.

This paper is published in full in this issue of the ARCHIVES, page 817.

VARIED SURGICAL INDICATIONS OF PTOSIS. DR. EDMUND B. SPAETH.

The various operative indications in any case of ptosis are the factors which modify the type of operation to be used. No one procedure can or will answer more than one set of indications and conditions. Therefore, it is necessary to utilize various procedures: those involving the occipito-frontalis muscle and at other times the superior rectus muscle or the superior oblique muscle in the direction of the ptosis. (Lantern slides were shown demonstrating the appearance before and after correction in representative cases.)

Jan. 19, 1939

FINAL OCULAR RESULT IN A CASE OF ANTERIOR CEREBELLAR-BULBAR-PONTILE POLIOMYELOENCEPHALITIS, TWENTY-SEVEN YEARS AFTER THE ACUTE ATTACK. DR. EDWARD A. SHUMWAY.

A woman, aged 33 was admitted to the University Hospital in September 1911, to the service of Dr. Charles K. Mills, at that time professor of neurology in the University of Pennsylvania. Neurologic examination showed complete paralysis of the left facial nerve and right hemiplegia. The tongue deviated to the right and the jaw to the left. There was paralysis also of the fifth and sixth cranial nerves and of the associated movements of the eyes, both to the right and to the left and up and down.

Ocular examination showed slight reduction of vision but entirely normal eyegrounds.

Dr. Mills' final diagnosis as the result of observations extending over years was "poliomyelitis, destructive, cerebellar-bulbar and pontile."

For a time the presence of a tumor was considered, and operation was at one time discussed, but the idea was dismissed. The patient had been under my care in my private practice for twenty-seven years.

As a result of the paralysis of the sixth nerve, which, with the involvement of the seventh nerve, remained permanent, and the weakness of the associated movements, both lateral and vertical, right hyperphoria and esotropia had developed. The hyperphoria had increased from 2 to 6 degrees as a result of the turning upward and inward of the left eye. The esophoria had decreased from 8 to 6 degrees. After final stabilization of the muscular condition, the patient was made comfortable with 3 degree prisms, base up in the left eye and base down in the right eye, for distance and prisms of 2 degrees in the same positions in each eye for reading. The esophoria did not need correction, and the patient was free from diplopia, both for distance and for near vision.

The final report of the neurologic condition, by Dr. J. W. McConnell, made a few days before this meeting, showed absence of sensory paralyses; recovery from the right hemiplegia, except for some hyperactivity of the deep reflexes on the right side, and permanent paralysis of the left facial nerve, which had been partly relieved by suturing the eyelids at the outer canthus. Finally, as a remaining sign

of bulbar involvement there was paresis of the left half of the vocal cords, which was confirmed by Dr. Ralph Butler and was due to a motor disturbance of the left recurrent laryngeal nerve.

DISCUSSION

DR. WALTER I. LILLIE: Dr. Shumway is to be envied in having had the privilege of observing such a case over a period of twenty-seven years. It does not fall to one's lot to be able to do this often. The case is obviously one of poliomyelitis, because of the history and the fact that the residual defects are entirely motor. Localization is obviously correct, because it included DeFoville's syndrome, which is paralysis of the sixth and seventh nerves with contralateral hemiplegia. The patient had also a homolateral Horner's syndrome, which fits into this picture. It has always been interesting that these patients do not have involvement of the eighth nerve, in spite of the fact that auditory nuclei are situated in the vicinity of the lesion. I believe that if the hearing could be examined like the visual fields, a homonymous hearing defect would be found in a case of this sort.

DR. EDWARD A. SHUMWAY: I think that I should mention Dr. Butler's report in regard to the ears.

He said that at present the patient's hearing on the left side is four tenths of normal and that this deafness is due to involvement of the middle ear, probably the result of a former suppurative inflammation, as there is a scar on the ear drum. Deafness may have been due to involvement of the eighth nerve, however, as Dr. Lillie has suggested.

My reasons for presenting this case are to report the ability to make the patient comfortable from an ophthalmologic point of view by the use of vertical prisms and to stimulate interest among ophthalmologists in neuro-ophthalmology.

ADIE'S SYNDROME: REPORT OF A CASE. DR. HAROLD G. SCHEIE.

It is important to recognize Adie's syndrome and to differentiate it from tabes dorsalis with Argyll Robertson pupils. Since in the case observed by me the pupil contracted well with physostigmine sulfate and was sensitized to choline compounds, it was felt that a partial denervation of the sphincter might have occurred.

DISUSSION

DR. FRANCIS HEED ADLER: Kinnier Wilson stated that no one should make a diagnosis of Argyll Robertson pupils unless he had read Argyll Robertson's original paper. It is certain that the diagnosis of Argyll Robertson pupils has been incorrect many times because all of the characteristics of this phenomenon were not strictly adhered to. Adie's syndrome is a case in point. One cannot be certain at the present time where the site of the lesion is in cases of Adie's syndrome, but with the help of animal experimentation it is possible that Dr. Scheie will be able to locate it more accurately.

DR. WARREN S. REESE: Are patients with this syndrome entirely symptomless?

DR. I. S. TASSMAN: Was the patient's accommodation tested after the use of choline?

DR. HAROLD G. SCHEIE: The patient has no symptoms, because only the ciliary muscle of one side is affected. If both sides were affected, the patient would certainly complain of blurring with changing the distance of his gaze.

This patient was tested before and after the use of choline, but I found little or no change from its use.

VARIOUS TYPES OF OCULAR MOVEMENTS: THEIR CLINICAL SIGNIFICANCE. DR. A. BIELSCHOWSKY, Hanover, N. H.

There are four main groups of ocular movements: the voluntary (commanded) movements; the attraction movements, which are brought about by sensorial stimuli attracting attention; the fusion movements, and the reflex movements of vestibular origin. The second and third groups are called psycho-optic reflexes because they take place almost automatically, without awareness of intention on the part of the subject; however, they are not true reflexes, as they are elicited by sensorial stimuli only if the latter attract attention.

Through error, doubts have been expressed as to the strict validity of the law according to which under normal conditions every innervation flows equally to the two eyes. The fact that a single eye can be moved separately does not prove that the unilateral movement is produced by a unilateral innervation. If two impulses are sent to the eyes simultaneously, one driving them in the same direction and the other in the opposite direction, an unequal or even unilateral movement must result. An ocular movement is never brought about by one single muscle. All the ocular muscles always cooperate in performing any ocular movement, one half acting as agonists and the other as antagonists. The same cortical center which controls the contraction of the agonists brings about the active relaxation of the antagonists, so that a movement may take place even if the agonists are unable to obey this motor impulse because of total paralysis.

Fusion movements are important for the visual act, particularly in persons with heterophoria, which can be kept latent only as long as the fusion mechanism maintains the innervation compensating the anomalous position of the eyes relative to each other.

The only true reflex movements of the eyes originate in the vestibular apparatus. Every change of the position of the head or body causing a current of the endolymph in the semicircular canals causes a stimulation which is conveyed to the motor nuclei by the posterior longitudinal bundle. The reaction of the ocular muscles aims at keeping the position of the eyes in space unaltered, notwithstanding the change of the position of the head or body.

A characteristic vestibular reaction is presented by the parallel rotary movement of the eyes around their anteroposterior axes, elicited by the tilting of the head toward the opposite side. This reaction is at the basis of ocular torticollis, which in cases of palsy of the trochlear

nerve and other disturbances of the oblique muscles helps the patient to see single. The head tilting test (Bielschowsky and Hofmann) is described as a method of diagnosing disturbances of the vertical motor muscles of the eyes.

The reaction of the eyes to vestibular stimuli is most important in cases of palsy of the supranuclear type. Failure of the muscles to respond to voluntary impulses while they react to vestibular stimuli produced by my head rotation test or by Bárány's test is proof that the nuclei and the peripheral nerve fibers are intact. (The characteristics of attraction or following movements were discussed with regard to those cases of palsy of the supranuclear type in which only the following movements are obtainable. The importance of Bell's phenomenon was illustrated by reports of cases of paralysis of the associated upward movement in which this phenomenon was the only proof of the supranuclear site of the lesion.) According to the particulars which can be ascertained by the various methods of investigation, it may be possible to make an approximate localization of the lesion causing the associated paralysis in an individual case.

Book Reviews

Die erblichen Hornhautdystrophien. Dystrophiae corneae hereditariae. By Prof. Dr. Max Bücklers, Tübingen. Price, 6.80 marks. Pp. 143, with 86 illustrations, 12 family trees and 3 tabulations. Stuttgart: Ferdinand Enke, 1938.

In this exhaustive publication Bücklers presents a study of 129 personal cases of hereditary corneal dystrophy, observed in and around Württemberg, a country in Southern Germany comparable in size and population with New Jersey. He has uncovered 12 family trees, some going back to the middle of the seventeenth century and comprising 300 persons. This rich material has been thoroughly sifted, and as a result of his painstaking studies the author was able to settle definitely some pertinent questions.

The conclusions arrived at by him are here presented.

All hereditary corneal dystrophies can be reduced to three independent pathologic conditions: (1) granular (nodular) corneal dystrophy (dystrophia corneae granularis [Groenouw I, Fleischer and others]); (2) macular corneal dystrophy (dystrophia corneae macularis [Groenouw II, Fuchs, Fehr, Fleischer and others]), and (3) lattice-like corneal dystrophy (dystrophia corneae reticulata [Haab, Dimmer and others]).

1. Granular corneal dystrophy is a dominant hereditary disease, beginning in the first decade of life in the form of minute changes visible only by the slit lamp. Later these changes become larger. They occupy a disklike area corresponding to a pupil of medium width. The intermediate tissue and a marginal zone always remain clear. Visual acuity does not suffer much, and what impairment there is occurs later in life; because of this, patients need not be sterilized.

2. Macular corneal dystrophy is a recessive hereditary disease. It, also, begins in the first ten years of life as a more or less diffuse and more rapidly progressing opacity of the whole cornea. The changes are macroscopically visible between the twentieth and the thirtieth year of life; they are of a more diffuse character than in the granular variety and impair the vision much more. Persons affected with macular dystrophy are to be sterilized.

3. Lattice-like corneal dystrophy is a dominant hereditary disease. It, too, begins in the first decade of life. In contrast to the opacities of the two other varieties, optical disturbances (lacunar formations or hyaline ridges) are responsible for its "lattice fibers." Later a disciform opacity may form in the center. Abrasions of the cornea are frequent. The surface becomes irregular early in youth, and vision suffers accordingly. The lattice-like dystrophy is much rarer than either the granular or the macular type. Persons suffering from the lattice-like type should be sterilized.

Hereditary corneal dystrophies all begin in early childhood and are always binocular. Both sexes are equally affected.

The opacities develop simultaneously in the two eyes and are frequently symmetric. They progress and resist all medication.

There are no transitional forms between the three types of corneal hereditary dystrophy, neither in the same person nor in the same family. There is no connection between these corneal dystrophies and other hereditary conditions.

The numerous pictures which adorn the book, some in color and most of them enlarged and somewhat overdone in order to show more impressively the essential clinical features, are especially valuable when they demonstrate the earliest stages of the disease, which are easily overlooked; the importance of the slit lamp in the study of these early phases is stressed.

A short discussion of all the reported cases precedes the description of the author's own cases. The various inefficient therapeutic measures are recorded. The microscopic anatomic picture of the lesions will be dealt with in a later publication.

A complete bibliography concludes the book, the acquisition of which is highly commended to anybody who is interested in one of the most engaging pathologic conditions of the cornea.

ERNST WALDSTEIN.

Anais da Faculdade de Medicina de Pôrto Alegre. Volume 1, July-September, 1938. Rio Grande do Sul, Brazil: Universidade de Pôrto Alegre.

The first number of a new quarterly journal has recently appeared which is published by the members of the Faculty of Medicine of Pôrto Alegre. In this number of 300 pages there are two articles by ophthalmologists.

The first article is by Dr. H. Arruga on the treatment of detachment of the retina. He considers the fundamental principle of all operative methods for this condition to be Gonin's great discovery that the tear should be closed. The percentage of recoveries with this method has been increased from 25 to 75 per cent in a few years. In cases in which no tear can be determined the detachment results from a choroidal exudate, and the treatment consists in removal of the inflammatory cause.

There are two important methods for localization. With the first, a blunt diathermy tip is used to make a small area of coagulation on the sclera which can be recognized with the ophthalmoscope. With the second method, that of Weve, a mark is made on the sclera at the place where the ophthalmoscope illuminates the pathologic retinal area. In general, the blunt diathermy tip is now preferred, and the sharp electrode is used only to facilitate the escape of the subretinal fluid.

With the new methods of operating, satisfactory results have been obtained in cases of extensive tears in the periphery of the retina, in cases of detachment at the ora serrata and in cases of holes in the macular region. The author has operated on 810 patients, with 396 clinical cures.

The second article is by Prof. Corrêa Meyer and deals with biologic problems of hereditary conditions in ophthalmology. He gives a general survey on the present knowledge of heredity based on the investigations of authors from Mendel to Morgan. The hereditary diseases in man are described, particularly as to their forms of heredity in connection with ophthalmology.

The conception of abiotrophy is particularly studied. According to the author, in such cases lethal semilethal factors are transmitted directly according to the mendelian law, whereby the cells of greatest development are first attacked and undergo a premature degeneration.

Finally, the author discusses from social standpoints the question of the prevention of hereditary diseases.

ARNOLD KNAPP.

Manual de enfermedades de los ojos. By Prof. Carlos E. Finlay, with the collaboration of Thomas Yanes, M.D. Pp. 664, with 275 black and white illustrations and 19 color plates. Habana, Cuba: "Cultural," S. A., 1939.

This manual, the author claims, has been written mostly for the benefit of medical students, general practitioners and those commencing the study of ophthalmology. A series of lectures delivered to medical students by Professor Finlay has been used for the publication of this book, with the addition of a few chapters contributed by Dr. Yanes. The manual contains twenty chapters, written in clear style. The authors have not tried to be exhaustive but have presented only the fundamentals of ophthalmology. The classic surgical procedures have been dealt with in detail. Other less known surgical methods have been briefly mentioned.

The book contains 275 illustrations in black and white and 19 color plates. Many of the illustrations, especially the photographs, are original, taken of personally observed patients of Dr. Finlay and of some of his Cuban colleagues. The color illustrations of fundi have been taken from the Atlas of Oller and are well reproduced.

Dr. Finlay emphasizes that in order to institute therapeutic methods properly, a solid foundation of anatomy, physiology and histopathology should be laid. For this reason therapy has been dealt with more extensively than is generally found in manuals of this type.

The relation between ocular and general diseases, as well as those of the nervous system, are well and simply outlined. The chapters on refraction, ocular hygiene, workmen's injuries and ocular therapeutics are clearly and concisely dealt with by Dr. Yanes. Most of the chapter on anomalies of the muscles has been taken from the Duane translation of Fuchs's "Text-Book of Ophthalmology," for which acknowledgment is made.

This book is dedicated to the memory of Dr. Finlay's parents, Carlos J. Finlay and Adela Shine de Finlay, and to Prof. Herman Knapp, for whom Dr. Finlay has great admiration, their friendship dating back to the days when he was an assistant at the New York Ophthalmic and Aural Institute.

RAMÓN CASTROVIEJO.

Twelfth Annual Report of the Giza Memorial Ophthalmic Laboratory, Cairo, 1937. Price, 35 piasters. Pp. 150. Cairo: Schindler's Press, 1938.

In addition to the clinical work of the laboratory, Major F. H. Stewart is carrying on experimental work on the causation of trachoma and Dr. F. Maxwell Lyons is conducting a careful investigation into factors bearing on the causation and treatment of spring catarrh. During the Fifteenth International Ophthalmologic Congress, which was held in Cairo, Dec. 8-14, 1937, the laboratory was visited by many members. During 1937 two postgraduate courses were given on medical and surgical ophthalmology, and 565 pathologic specimens were examined. Among these there were 91 eyes lost as the result of purulent ophthalmia. There were 68 specimens showing malignant tumors and 76 showing lesions due to trachoma. The presence of eosinophils is not regarded as important for the diagnosis of spring catarrh in Egypt, while the thin glistening tenacious membrane which forms on the tarsal conjunctiva on exposure to the air is a most valuable clinical sign.

A number of interesting pathologic reports and reports of unusual clinical cases are given. The results of treating trachoma with sulfanilamide and primary glaucoma with extract of adrenal cortex were unsatisfactory. The appendix contains studies on the pathologic picture of experimental trachoma by F. H. Stewart and on the biomicroscopic picture of spring catarrh by F. Maxwell Lyons.

The director, Dr. Rowland P. Wilson, is to be congratulated on the continued excellence of the work done in this laboratory.

ARNOLD KNAPP.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. Stewart Duke-Elder, 59 Harley St., London, W. 1.
Secretary: Dr. Thomasina Belt, 13 Mitchell Ave., Jesmond, Newcastle-on-Tyne.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: T. Harrison Butler, 81 Edmund St., Birmingham, England.
Place: Birmingham and Midland Eye Hospital.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 81 Edmund St., Birmingham, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Road, Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Time: July 6-8, 1939.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

TSINAN OPHTHALMOLOGICAL SOCIETY

Chairman: Dr. Eugene Chan, Cheeloo University School of Medicine, Tsinan, Shantung, China.
Place: Cheeloo University School of Medicine. Time: Last Thursday of alternate months.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary: Dr. Derrick T. Vail Jr., 441 Vine St., Cincinnati.
Place: St. Louis. Time: May 15-19, 1939.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Chicago. Time: Oct. 8-13, 1939.

American Ophthalmological Society

President: Dr. Frederick Tooke, 1482 Mountain St., Montreal, Canada.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va.

Canadian Medical Association, Section on Ophthalmology

President: Dr. S. Hanford McKee, 1528 Crescent St., Montreal.
Secretary-Treasurer: Dr. J. A. MacMillan, 1410 Stanley St., Montreal.
Place: Montreal. Time: June 19-23, 1939.

National Society for the Prevention of Blindness

President: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.

SECTIONAL

Central Wisconsin Society of Ophthalmology and Otolaryngology

President: Dr. R. O. Ebert, 104 Main St., Oshkosh.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Oshkosh. Time: May 1939.

New England Ophthalmological Society

President: Dr. Edwin B. Goodall, 101 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. F. C. Cordes, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.
Place: San Francisco. Time: June 19-22, 1939.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. Edward Clark, 1305–14th Ave., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1115 Terry Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary-Treasurer: Dr. Thorsten E. Blomberg, 501–7th St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. Don M. Howell, Alma, Mich.
Secretary-Treasurer: Dr. Louis D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. R. A. Kelly, 304 N. Main St., Mitchell, S. D.
Secretary-Treasurer: Dr. J. C. Decker, 515 Frances Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

Southwestern Michigan Triological Society

President: Dr. Carl Wencke, Battle Creek.
Secretary-Treasurer: Dr. A. K. Zinn, Battle Creek.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. M. Harris, Johnstown.
Secretary-Treasurer: Dr. C. Wearne Beals, 41 N. Brady St., DuBois.

STATE

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward Jackson, 1008-A Republic Bldg., Denver.
Secretary: Dr. John C. Long, 324 Metropolitan Bldg., Denver.
Place: University Club, Denver. Time: 6:30 p. m., third Saturday of each month, October to April, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. William M. Good, 63 Center St., Waterbury.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. Grady E. Clay, 384 Peachtree St., N. E., Atlanta.
Secretary-Treasurer: Dr. J. Mason Baird, 511 Medical Arts Bldg., Atlanta.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. C. W. Rutherford, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Marlow W. Manion, 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: First Wednesday in April.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. H. H. Lamb, American Bank Bldg., Davenport.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.
Place: Davenport.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Francis E. Le Jeune, 632 Maison Blanche Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.
Place: Gulfport, Miss. Time: May 8, 1939.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. B. Fralick, 201 S. Main St., Ann Arbor.
Secretary: Dr. O. McGillicuddy, 124 W. Allegan St., Lansing.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Frank N. Knapp, 318 W. Superior St., Duluth.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Norman W. Burritt, 30 Beechwood Rd., Summit.
Secretary: Dr. A. Russell Sherman, 671 Broad St., Newark.
Place: Atlantic City. Time: June 1939.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Algernon B. Reese, 73 E. 71st St., New York.
Secretary: Dr. Chester C. Cott, 333 Linwood Ave., Buffalo.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. C. Smith, 106 W. 7th St., Charlotte.
Secretary-Treasurer: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Place: Statesville. Time: Sept. 21, 1939.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516-6th St., Valley City.
Place: Fargo. Time: May 1939.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. L. O. Clement, 406 State St., Salem.
Secretary-Treasurer: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. S. B. Fishburne, 1430 Marion St., Columbia.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. B. Stanford, 899 Madison Ave., Memphis.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. A. N. Champion, 705 E. Houston St., San Antonio.
Secretary: Dr. Dan Brannin, 1719 Pacific Ave., Dallas.
Place: Houston. Time: December 1939.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. V. P. White, 143½ S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. E. B. Fairbanks, Boston Bldg., Salt Lake City.
Time: Third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Charles T. St. Clair, 418 Bland St., Bluefield, W. Va.
Secretary-Treasurer: Dr. M. H. Williams, 30½ Franklin Rd., S. W., Roanoke.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Andrew Rados, 31 Lincoln Park, Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. L. E. Brown, Second National Bldg., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Anderson, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. Arthur G. Fort, 478 Peachtree St., N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St., N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Frank B. Walsh, Wilmer Institute, Johns Hopkins Hospital, Baltimore.
Secretary: Dr. Fred M. Reese, 6 E. Eager St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. N. E. Miles, 408 Medical Arts Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. E. Clifford Place, 59 Livingston St., Brooklyn.
Secretary-Treasurer: Dr. Frank Mallon, 1135 Park Pl., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Ivan J. Koenig, 40 North St., Buffalo.
Secretary-Treasurer: Dr. Meyer H. Riwchun, 367 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. A. H. Benz, 706 Medical Arts Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Georgiana Dvorak-Theobald, 715 Lake St., Oak Park, Ill.
Secretary-Treasurer: Dr. Earle B. Fowler, 55 E. Washington St., Chicago.
Place: Medinah Michigan Avenue Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Paul Moore, Republic Bldg., Cleveland.
Secretary: Dr. G. Leslie Miller, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. Hugh G. Beatty, 150 E. Broad St., Columbus, Ohio.
Secretary-Treasurer: Dr. W. A. Stoutenborough, 21 E. State St., Columbus, Ohio.
Place: Deshler Wallick Hotel. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Edgar G. Mathis, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. E. King Gill, 416 Chaparral St., Corpus Christi, Texas.
Time: Second Thursday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Maxwell Thomas, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. J. Dudley Singleton, 1719 Pacific Ave., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. E. G. Linn, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Arthur S. Hale, 1609 Eaton Tower, Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. A. Gough, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. Charles R. Lees, 806 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Dewey R. Heetderks, 405 Medical Arts Bldg., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Robert G. Laird, 116 E. Fulton St., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. Louis Daily, 1215 Walker Ave., Houston, Texas.
Secretary: Dr. Herbert H. Harris, 1004 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. J. K. Leasure, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to June.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. N. Robertson, Concordia, Kan.
Secretary: Dr. John S. Knight, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Ben K. Parks, 619 Professional Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. Paul Nilsson, 211 Cherry Ave., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Pierre Viole, 1930 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

LOUISVILLE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Gaylord C. Hall, Brown Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. Charles K. Beck, Starks Bldg., Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Earle Breeding, 1801 I St., N. W., Washington.
Secretary: Dr. Elmer Shepherd, 1606-20th St., N. W., Washington.
Place: 1718 M St., N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sonders, Medical Arts Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. John E. Mulsow, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

MINNEAPOLIS OPHTHALMOLOGICAL SOCIETY

Chairman: Each member, in alphabetical order.
Secretary: Dr. M. C. Pfunder, 645 Medical Arts Bldg., Minneapolis.
Place: Hennepin County Medical Society rooms. Time: 6:30 p. m., fourth Monday of each month, October to May, inclusive.

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. L. de G. Joubert, 690 Dunlop St., Montreal, Canada.
Secretary: Dr. K. B. Johnston, 1509 Sherbrooke St., W., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Guy Maness, 119–7th Ave., Nashville, Tenn.
Secretary-Treasurer: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. E. G. Walls, 619 Maison Blanche Bldg., New Orleans.
Secretary-Treasurer: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. James W. White, 15 Park Ave., New York.
Secretary: Dr. Rudolf Aebli, 30 E. 40th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Percy Fridenberg, 38 W. 59th St., New York.
Secretary: Dr. David Alperin, 889 Park Pl., Brooklyn.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. Philip Romonek, 107 S. 17th St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Ophthalmological Society of the University of Pittsburgh

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Time: Second Monday in November, January, March and May.

Passaic-Bergen Ophthalmological Club

President: Dr. R. N. Berke, 430 Union St., Hackensack, N. J.
Secretary-Treasurer: Dr. T. A. Sanfacon, 340 Park Ave., Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Edward Stieren, Union Trust Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Rudolph Thomason, Professional Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Edwin S. Ingersoll, 26 S. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 8 p. m., second Wednesday of each month from September to May.

St. Louis Ophthalmic Society

President: Dr. B. Y. Alvis, Carleton Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Oscar H. Judkins, 414 Navarro St., San Antonio, Texas.
Secretary-Treasurer: Dr. Wilfred E. Muldoon, 414 Navarro St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Russell Fletcher, 490 Post St., San Francisco.
Secretary: Dr. Avery Morley Hicks, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except May, June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. W. L. Atkins, 940 Margaret Pl., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. P. B. Greene, 422 Riverside Ave., Spokane, Wash.
Secretary: Dr. O. M. Rott, 421 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. James F. Cahill, 428 S. Salina St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. Herbert Katz, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. A. Lloyd Morgan, 170 St. George St., Toronto, Canada.
Secretary: Dr. W. R. F. Luke, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. G. Victor Simpson, 1710 Rhode Island Ave., N. W., Washington, D. C.
Secretary-Treasurer: Dr. Frank D. Costenbader, 1726 I St., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 8 p. m., first Monday in November, January, March and May.